

WORLD INTELLECTUAL PROPERTY ORGANIZATION International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)						
(51) International Patent Classification ⁶ :	A2	(11) International Publication Number: WO 98/55508				
C07K 14/00		(43) International Publication Date: 10 December 1998 (10.12.98)				
(21) International Application Number: PCT/JPS (22) International Filing Date: 3 June 1998 ((AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT,					
(22) mechanoral rung pate. 3 June 1996 (33.00.9	6) LO, NO, NE, F 1, SEJ.				
(30) Priority Data: 9/144948 3 June 1997 (03.06.97)	:	Published Without international search report and to be republished upon receipt of that report.				
(71) Applicants (for all designated States except US): S CHEMICAL RESEARCH CENTER [JP/JP Nishi-Ohnuma 4-chome, Sagamihara-shi, K 229-0012 (JP). PROTEGENE INC. [JP/JP]; Naka-cho, Meguro-ku, Tokyo 153-0065 (JP).	.1, va					
(72) Inventors; and (75) Inventors/Applicants (for US only): KATO, Seishi 3-46-50, Wakamatsu, Sagamihara-shi, K 229-0014 (JP). SEKINE, Shingo [JP/JP]; 101, 2-8-15, Atago, Ageo-shi, Saitama 362-00 YAMAGUCHI, Tomoko [JP/JP]; 5-13-11, T Katsushika-ku, Tokyo 125-0054 (JP).	va zu P).					
(74) Agents: AOYAMA, Tamotsu et al.; Aoyama & IMP Building, 3-7, Shiromi 1chome, Chuo-ku, O Osaka 540-0001 (JP).	rs, ni,					
	BKAN	E DOMAINS AND DNAS ENCODING THESE PROTEINS				
(57) Abstract						
Proteins comprising any of the amino acid sequences of the nucelotide sequences of SEQ ID NOS: 19 to 36 are		Q ID NOS: 1 to 18 and DNAs encoding said proteins and comprising any ed.				
X+						

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BR	Belgium	GN	Guinea	MK	The former Yugoslav	TM	Turkmenistan
BF	Burkina Faso	GR	Greece		Republic of Macedonia	TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IR	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	. MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Itały	MCX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	zw	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's	NZ	New Zealand		
CM	Cameroon		Republic of Korea	PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

1

DESCRIPTION

Human Proteins Having Transmembrane Domains and DNAs Encoding These Proteins

5

FIELD OF THE INVENTION

The present invention relates to human proteins having transmembrane domains and cDNAs encoding these proteins. The membrane proteins of this invention can be used as pharmaceuticals or as antigens for preparing antibodies against said proteins. The cDNAs of the invention can be used as probes for the gene diagnosis and gene sources for the gene therapy. The cDNAs can also be used as gene sources for large-scale production of the membrane proteins encoded by the same. The cells into which the genes encoding the membrane proteins are introduced for expression of such membrane proteins in large amounts can be used for detection of the corresponding ligands, screening of low molecular weight medicines, etc.

20 BACKGROUND OF THE INVENTION

Membrane proteins play important roles as signal receptors, ion channels, transporters, etc. for the material transportation or information transmission mediated by the cell membrane. For instance, they are known to serve as receptors for various cytokines, ion channels for sodium ion, potassium ion, chloride ion, etc., transporters for saccharides and amino acids, and so on. The genes for many of them have been cloned already.

In recent years, it was clarified that the abnormalities

WO 98/55508

15

PCT/JP98/02445

of these membrane proteins are related to a number of hitherto cryptogenic diseases. For example, a gene for a membrane protein having 12 transmembrane domains was identified as the qene responsible for cystic fibrosis (Rommens, J. M. et al., 5 Science 245: 1059-1065 (1989)]. It was also clarified that several membrane proteins act as the receptors when a virus infects the cells. For example, HIV-1 was revealed to infect into the cells through the mediation of a membrane protein fusin, a membrane protein on the T-cell membrane, having a CD-4 10 antigen and 7 transmembrane domains [Feng, Y. et al., Science 272: 872-877 (1996)]. Therefore, the discovery of new membrane proteins is anticipated to lead to the elucidation of the causes of many diseases, and the isolation of new genes coding for the membrane proteins is desired.

2

Heretofore, owing to the difficulty in their purification, many of membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises transfection of a cDNA library in the animal cells to express the cDNA and detection 20 of the cells expressing the target membrane protein on the membrane by an immunological technique using an antibody or a physiological technique for the change in the membrane permeability. However, this method is applicable only to cloning of a gene for a membrane protein with a known function.

25 In general, membrane proteins possess hydrophobic transmembrane domains inside the proteins which are synthesized in the ribosome. Said domains remain in the phospholipid to be trapped in the membrane. Accordingly, the evidence of the cDNA for encoding the membrane protein is provided by determination

3 .

of the whole base sequence of a full-length cDNA and detection of highly hydrophobic transmembrane domains in the amino acid sequence of the protein encoded by said cDNA.

As a result of the extensive study, there have successfully been obtained human proteins having transmembrane domains, particularly comprising any of the amino acid sequences of SEQ ID NOS: 1 to 18, by cloning cDNAs coding for proteins having transmembrane domains, particularly comprising any of the nucleotide sequences of SEQ ID NOS: 19 to 36, from a human 10 full-length cDNA bank. The present invention is based on the above success.

SUMMARY OF THE INVENTION

15

A main object of the present invention is to provide novel human proteins having transmembrane domains, particularly comprising any of the amino acid sequences of SEQ ID NOS: 1 to 18. Another object of this invention is to provide DNAs coding for said novel proteins, particularly comprising any of the nucleotide sequences of SEQ ID NOS: 19 to 36. A further object 20 of the invention is to provide expression vectors capable of in vitro translating said DNAs or expressing said DNAs in eukaryotic cells. A still further object of the invention is to provide transformed eukaryotic cells capable of expressing said DNAs to produce said proteins.

25 In one embodiment, the present invention provides a composition comprising a protein, wherein said protein comprises an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ ID NOS: 1 to 18 and their fragments.

In another embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.

In a further embodiment, the present invention provides a composition comprising an isolated polynucleotide selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.

10 BRIEF DESCRIPTION OF DRAWINGS

- Figure 1: A figure depicting the structure of the secretory signal sequence detection vector pSSD3.
- Figure 2: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01263.
- 15 Figure 3: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01299.
 - Figure 4: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01347.
- Figure 5: A figure depicting the hydrophobicity/hydrophi-20 licity profile of the protein encoded by clone HP01440.
 - Figure 6: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01526.
 - Figure 7: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10230.
- 25 Figure 8: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10389.
 - Figure 9: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10408.
 - Figure 10: A figure depicting the hydrophobicity/hydro-

5

philicity profile of the protein encoded by clone HP10412.

Figure 11: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10413.

Figure 12: A figure depicting the hydrophobicity/hydro-5 philicity profile of the protein encoded by clone HP10415.

Figure 13: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10419.

Figure 14: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10424.

10 Figure 15: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10428.

Figure 16: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10429.

Figure 17: A figure depicting the hydrophobicity/hydro15 philicity profile of the protein encoded by clone HP10432.

Figure 18: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10433.

Figure 19: A figure depicting the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10480.

20

BEST MODE FOR CARRING OUT INVENTION

The proteins of the present invention can be obtained, for example, by isolation from human organs, cell lines, etc., by chemical synthesis on the basis of the amino acid sequences as herein disclosed, or by recombinant DNA technology using the DNA encoding the transmembrane domains of the invention. Among them, adoption of the recombinant DNA technology is preferred. Specifically, each of the proteins may be prepared by in vitro transcription of a vector comprising the cDNA of the invention

to make RNA and in vitro translation using this RNA as a template to accomplish in vitro expression. Also, each of the proteins may be prepared in a large amount by the use of Escherichia coli, Bacillus subtilis, yeasts, animal cells, etc. 5 comprising a suitable expression vector having the DNA encoding such protein.

In the case of producing the protein of the invention by the use of a microorganism such as Escherichia coli, the translation region of the cDNA of the invention is constructed in an expression vector having an origin, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator, etc. that can be replicated in the microorganism and, after transformation of the host cells with said expression vector, the resultant transformant is incubated, whereby the protein 15 encoded by said cDNA can be produced in a large amount in the microorganism. In that case, a protein fragment containing an optional region can be obtained by performing the expression with inserting an initiation codon and a termination codon before and after the optional translation region. Alternative-20 ly, a fusion protein with another protein can be expressed. Only a protein portion encoding said cDNA can be obtained by cleavage of said fusion protein with an appropriate protease.

10

For production of the protein of the invention by expression of DNA coding for such protein in eukaryotic cells, 25 the translation region of said cDNA may be recombined into an expression vector for eukaryotic cells having a promoter, a splicing domain, a poly(A) addition site, etc., followed by introduction into eukaryotic cells so that the protein of the invention is produced as a membrane protein on the cell

membrane surface. Examples of the expression vector are pKA1, pED6_dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, etc. As the eukaryotic cells, there are exemplified mammalian animal culture cells (e.g. simian kidney 5 cells COS7, chinese hamster ovary cells CHO), budding yeasts, Schizosaccharomyces pombe, silkworm cells, Xenopus laevis egg cells, etc., but any other eukaryotic cells may also be used insofar as the protein of the invention can be expressed on the membrane surface. In order to introduce the expression vector 10 into eukaryotic cells, there may be adopted any conventional procedure such as electroporation, calcium phosphate method, liposome method or DEAE dextran method.

The proteins of the present invention include peptide fragments (5 or more amino acid residues) containing any 15 partial amino acid sequence of the amino acid sequences of SEQ ID NOS: 1 to 18. These fragments can be used as antigens for preparation of the antibodies. Also, the proteins of the invention that have signal sequences appear in the form of maturation proteins on the cell surface, after the signal 20 sequences are removed. Therefore, these maturation proteins shall come within the scope of the present invention. The Nterminal amino acid sequences of the maturation proteins can be easily identified by using the method for the cleavage-site determination in a signal sequence [Japan Patent Kokai No. 187100/96]. Further, many membrane proteins are subjected to the processing on the cell surface to be converted to the secretor forms. These secretor proteins or peptides shall come within the scope of the present invention. When glycosylation sites are present in the amino acid sequences, expression in

25

PCT/JP98/02445 WO 98/55508

8

appropriate animal cells affords glycosylated proteins. Therefore, these glycosylated proteins or peptides also shall come within the scope of the invention.

The DNAs of the invention include all DNAs encoding the above-mentioned proteins. Said DNAs can be obtained using the method by chemical synthesis, the method by cDNA cloning, and so on.

Each of the cDNAs of the invention can be cloned from, for example, the cDNA libraries of the human cell origin. The cDNA 10 is synthesized using as a template a poly(A) + RNA extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the culture cells. The cDNA can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, 15 P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)] as illustrated in Examples in order to obtain a full-length clone in an effective manner.

The primary selection of a cDNA encoding a human protein having transmembrane domains is performed by the sequencing of a partial base sequence of the cDNA clone selected at random from the cDNA libraries, sequencing of the amino acid sequence encoded by the base sequence, and recognition of the presence 25 or absence of hydrophobic site(s) in the resulting N-terminal amino acid sequence region. Next, the secondary selection is carried out by determination of the whole base sequence by the sequencing and the protein expression by the in vitro translation. The ascertainment of the cDNA of the present

20

9

invention for encoding the protein having the secretory signal sequence is performed by using the signal sequence detection method [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. In other words, the ascertainment for the coding portion of the inserted cDNA fragment to function as a signal sequence is provided by fusing a cDNA fragment encoding the N-terminus of the target protein with a cDNA encoding the protease domain of urokinase and then expressing the resulting cDNA in COS7 cells to detect the urokinase activity in the cell culture medium. On the other hand, the N-terminal region is judged to remain in the membrane in the case where the urokinase activity is not detected in the cell culture medium.

The cDNAs of the invention are characterized by containing any of the nucleotide sequences of SEQ ID NOS: 19 to 36 or any of the nucleotide sequences of SEQ ID NOS: 37 to 54. Table 1 summarizes the clone number (HP number), the cells affording the cDNA, the total nucleotide number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

10

Table 1

Sequence Number	HP Number	Cells	Number of Nucleotides	Number of Amino Acid Residues
1, 19, 37	HP01263	Liver	1502	382
2, 20, 38	HP01299	Liver	1349	317
3, 21, 39	HP01347	Liver	1643	296
4, 22, 40	HP01440	Stomach cancer	729	197
5, 23, 41	HP01526	Stomach cancer	1322	221
6, 24, 42	HP10230	Stomach cancer	3045	251
7, 25, 43	HP10389	КВ	653	106
8, 26, 44	HP10408	Stomach cancer	439	78
9, 27, 45	HP10412	Stomach cancer	1131	314
0, 28, 46	HP10413	Stomach cancer	1875	195
1, 29, 47	HP10415	Stomach cancer	1563	462
2, 30, 48	HP10419	Stomach cancer	2030	247
3, 31, 49	HP10424	Stomach cancer	493	113
4, 32, 50	HP10428	КВ	2044	365
.5, 33, 51	HP10429 ·	Stomach cancer	1043	226
.6, 34, 52	HP10432	Liver	972	129
.7, 35, 53	HP10433	Liver	695	163
.8, 36, 54	HP10480	Stomach cancer	1914	193
	Number 1, 19, 37 2, 20, 38 3, 21, 39 4, 22, 40 5, 23, 41 6, 24, 42 7, 25, 43 8, 26, 44 9, 27, 45 0, 28, 46 1, 29, 47 2, 30, 48 3, 31, 49 4, 32, 50 5, 33, 51 6, 34, 52 7, 35, 53	Number Number 1, 19, 37 HP01263 2, 20, 38 HP01299 3, 21, 39 HP01347 4, 22, 40 HP01440 5, 23, 41 HP01526 6, 24, 42 HP10230 7, 25, 43 HP10389 8, 26, 44 HP10408 9, 27, 45 HP10412 0, 28, 46 HP10413 1, 29, 47 HP10415 2, 30, 48 HP10419 3, 31, 49 HP10424 4, 32, 50 HP10428 5, 33, 51 HP10429 6, 34, 52 HP10432 7, 35, 53 HP10433	Number Number 1, 19, 37 HP01263 Liver 2, 20, 38 HP01299 Liver 3, 21, 39 HP01347 Liver 4, 22, 40 HP01440 Stomach cancer 5, 23, 41 HP01526 Stomach cancer 6, 24, 42 HP10230 Stomach cancer 7, 25, 43 HP10389 KB 8, 26, 44 HP10408 Stomach cancer 9, 27, 45 HP10412 Stomach cancer 0, 28, 46 HP10413 Stomach cancer 1, 29, 47 HP10415 Stomach cancer 2, 30, 48 HP10419 Stomach cancer 3, 31, 49 HP10424 Stomach cancer 4, 32, 50 HP10428 KB 5, 33, 51 HP10429 Stomach cancer 6, 34, 52 HP10432 Liver 7, 35, 53 HP10433 Liver	Number Number Nucleotides 1, 19, 37 HP01263 Liver 1502 2, 20, 38 HP01299 Liver 1349 3, 21, 39 HP01347 Liver 1643 4, 22, 40 HP01440 Stomach cancer 729 5, 23, 41 HP01526 Stomach cancer 1322 6, 24, 42 HP10230 Stomach cancer 3045 7, 25, 43 HP10389 KB 653 8, 26, 44 HP10408 Stomach cancer 439 9, 27, 45 HP10412 Stomach cancer 1131 0, 28, 46 HP10413 Stomach cancer 1563 2, 30, 48 HP10419 Stomach cancer 2030 3, 31, 49 HP10424 Stomach cancer 493 4, 32, 50 HP10428 KB 2044 5, 33, 51 HP10429 Stomach cancer 1043 6, 34, 52 HP10432 Liver 972 7, 35, 53 HP10433 Liver 695

45

Hereupon, the same clone as any of the cDNAs of the invention can be easily obtained by screening of the cDNA libraries constructed from the cell line or the human tissues employed in the invention, by the use of an oligonucleotide.

50 probe synthesized on the basis of the corresponding cDNA nucleotide sequence of SEQ ID NOS: 37 to 54.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Therefore, any cDNA that is subjected to insertion or deletion of one or plural nucleotides and/or substitution with other nucleotides

11

in SEQ ID NOS: 37 to 54 shall come within the scope of the invention.

In a similar manner, any protein that is produced by these modifications comprising insertion or deletion of one or plural 5 nucleotides and/or substitution with other nucleotides shall come within the scope of the present invention, as far as said protein possesses the activity of the corresponding protein having the amino acid sequence of SEQ ID NOS: 1 to 18.

The cDNAs of the invention include cDNA fragments (more than 10 bp) containing any partial nucleotide sequence of the nucleotide sequence of SEQ ID NOS: 19 to 36 or of the nucleotide sequence of SEQ ID NOS: 37 to 54. Also, DNA fragments consisting of a sense chain and an anti-sense chain shall come within this scope. These DNA fragments can be used 15 as the probes for the gene diagnosis.

10

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are 20 derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or 25 suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or primers from the disclosed sequence information for identification and/or amplification of genes in appropriate

12

genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

5 Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave 10 the mRNA transcribed from the gene (Albert and Morris, 1994, Trends Pharmacol. Sci. 15(7): 250-254; Lavarosky et al., 1997, Biochem. Mol. Med. 62(1): 11-22; and Hampel, 1998, Prog. Nucleic Acid Res. Mol. Biol. 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that 15 have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified 20 genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 Bl, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to 25 the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished through

13

insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the 15 corresponding gene(s), and for the development of assay systems for the identi fication of molecules that interact with the protein product(s) of the corresponding gene(s).

Where the protein of the present invention membrane-bound (e.g., is a receptor), the present invention 20 also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be 25 identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at

WO 98/55508

15

least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined 5 by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, 10 most preferably 30 or more) contiquous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of 20 skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides proteins; that or is, naturally-occurring alternative forms of the polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences

15

complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably being the stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example,

Table 2

Stringency	Polynucleotide	Hybrid	Hybridization Temperature	Wash
Condition	Hybrid	Length	and Buffer [†]	Temperature
		(bp) [‡]		and Buffer [†]
A	DNA : DNA	≥50	65℃; 1×SSC -or-	65℃; 0.3×SSC
			42℃; 1×SSC,50% formamide	
В	DNA : DNA	<50	T _B *; 1×SSC	T _B *; 1×SSC
C	DNA : RNA	≥50	67℃; 1×SSC -or-	67℃; 0.3×SSC
			45℃; 1×SSC,50% formamide	
D	DNA : RNA	<50	T _D *; 1×SSC	T _D *; 1×SSC
E	RNA: RNA	≥50	70℃; 1×SSC -or-	70℃; 0.3×SSC
	·		50℃; 1×SSC,50% formamide	
F	RNA: RNA	<50	T _F *; 1×SSC	T _F *; 1×SSC
G	DNA : DNA	≥50	65℃; 4×SSC -or-	65℃; 1×SSC
			42℃; 4×SSC,50% formamide	
H	DNA : DNA	<50	T _H *; 4×SSC	T _H *; 4×SSC
I	DNA: RNA	≥50	67℃; 4×SSC -or-	67℃; 1×SSC
			45°C; 4×SSC,50% formamide	
J	DNA: RNA	<50	T _J *; 4×SSC	T _J *; 4×SSC
K	RNA: RNA	≥50	70℃; 4×SSC -or-	67℃; 1×SSC
			50°C; 4×SSC,50% formamide	
L	RNA: RNA	<50	T _L *; 2×SSC	T _L *; 2×SSC
M	DNA : DNA	≥50	50℃; 4×SSC -or-	50°C; 2×SSC
			40℃; 6×SSC,50% formamide	
N	DNA : DNA	<50	T _N *; 6×SSC	T _N *; 6×SSC
О	DNA: RNA	≥50	55℃; 4×SSC -or-	55℃; 2×SSC
			42°C; 6×SSC,50% formamide	
P	DNA : RNA	<50	T _P *; 6×SSC	Tp*; 6×SSC
Q	RNA: RNA	≥50	60℃; 4×SSC -or-	60°C; 2×SSC
			45°C; 6×SSC,50% formamide	
R	RNA: RNA	<50	T _R *; 4×SSC	T _R *; 4×SSC

- ‡: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.
- †: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH₂PO₄, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.
- * T_B T_R : The hybridization temperature for hybrids anticipated to be less than 50 base pairs in length should be 5-10°C less than the melting temperature (T_m) of the hybrid, where T_m is determined according to the following equations. For hybrids less than 18 base pairs in length, T_m (°C)=2(#of A + T bases) + 4(# of G + C bases). For hybrids between 18 and 49 base pairs in length, T_m (°C)=81.5 + 16.6(log₁₀[Na⁺]) + 0.41 (%G+C) (600/N), where N is the number of bases in the hybrid, and [Na⁺] is the concentration of sodium ions in the hybridization buffer ([Na⁺] for 1×SSC=0.165M).

17

Additional examples of stringency conditions for polynucleotide hybridization are

provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory

5 Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and

Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc.,

sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more

preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of

the present invention to which it hybridizes, and has at least

15 60% sequence identity (more

preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the

polynucleotide of the present invention to which it hybridizes, where sequence identity is

20 determined by comparing the sequences of the hybridizing polynucleotides when aligned so as

to maximize overlap and identity while minimizing sequence gaps.

25 EXAMPLE

The present invention is embodied in more detail by the following examples, but this embodiment is not intended to restrict the present invention. The basic operations and the enzyme reactions with regard to the DNA recombination are

18

Carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989].

Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo Co., Ltd. The manufacturer's instructions were used for the buffer compositions as well as for the reaction conditions, in each of the enzyme reactions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

10 (1) Preparation of Poly(A) + RNA

The epidermoid carcinoma cell line KB (ATCC CRL 17), tissues of stomach cancer delivered by the operation, and liver were used for human cells to extract mRNAs. The cell line was cultured by a conventional procedure.

of a 5.5 M guanidinium thiocyanate solution, total mRNAs were prepared in accordance with the literature [Okayama, H. et al., "Methods in Enzymology" Vol. 164, Academic Press, 1987]. These mRNAs were subjected to chromatography using an oligo(dT)-cellulose column washed with 20 mM Tris-hydrochloric acid buffer solution (pH 7.6), 0.5 M NaCl, and 1 mM EDTA to obtain a poly(A)⁺ RNA in accordance with the above-mentioned literature.

(2) Construction of cDNA Library

To a solution of 10 μg of the above-mentioned poly(A)⁺ RNA in 100 mM Tris-hydrochloric acid buffer solution (pH 8) was added one unit of an RNase-free, bacterium-origin alkaline phosphatase and the resulting solution was allowed to react at 37°C for one hour. After the reaction solution underwent the

WO 98/55508

PCT/JP98/02445

phenol extraction followed by the ethanol precipitation, the obtained pellets were dissolved in a mixed solution of 50 mM sodium acetate (pH 6), 1 mM EDTA, 0.1% 2-mercaptoethanol, and 0.01% Triton X-100. Thereto was added one unit of a tobacco-origin pyrophosphatase (Epicenter Technologies) and the resulting solution at a total volume of 100 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a decapped poly(A)⁺ RNA solution.

19

To a solution of the decapped poly(A)⁺ RNA and 3 nmol of a DNA-RNA chimeric oligonucleotide (5'-dG-dG-dG-dG-dA-dA-dT-dT-dC-dG-dA-G-G-A-3') in a mixed aqueous solution of 50 mM Trishydrochloric acid buffer solution (pH 7.5), 0.5 mM ATP, 5 mM MgCl₂, 10 mM 2-mercaptoethanol, and 25% polyethylene glycol were added 50 units of T4 RNA ligase and the resulting solution at a total volume of 30 µl was allowed to react at 20°C for 12 hours. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in water to obtain a chimeric oligo-capped poly(A)⁺ RNA.

After the vector pKA1 developed by the present inventors (Japanese Patent Kokai Publication No. 1992-117292) was digested with KpnI, an about 60-dT tail was inserted by a terminal transferase. This product was digested with EcoRV to remove the dT tail at one side and the resulting molecule was used as a vectorial primer.

After 6 μg of the previously-prepared chimeric oligocapped poly(A)[†] RNA was annealed with 1.2 μg of the vectorial

20

primer, the product was dissolved in a mixed solution of 50 mM Tris-hydrochloric acid buffer solution (pH 8.3), 75 mM KCl, 3 mM MgCl₂, 10 mM dithiothreitol, and 1.25 mM dNTP (dATP + dCTP + dGTP + dTTP), mixed with 200 units of a reverse transferase (GIBCO-BRL), and the resulting solution at a total volume of 20 μl was allowed to react at 42°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol precipitation, the thus-obtained pellets were dissolved in a mixed solution of 50 mM Tris-hydrochloric acid 10 buffer solution (pH 7.5), 100 mM NaCl, 10 mM MgCl $_2$, and 1 mM dithiothreitol. Thereto were added 100 units of EcoRI and the resulting solution at a total volume of 20 µl was allowed to react at 37°C for one hour. After the reaction solution underwent the phenol extraction followed by the ethanol 15 precipitation, the obtained pellets were dissolved in a mixed solution of 20 mM Tris-hydrochloric acid buffer solution (pH 7.5), 100 mM KCl, 4 mM MgCl₂, 10 mM (NH₄)₂SO₄, and 50 μ g/ml bovine serum albumin. Thereto were added 60 units of Escherichia coli DNA ligase and the resulting solution was 20 allowed to react at 16°C for 16 hours. To the reaction solution were added 2 µl of 2 mM dNTP, 4 units of Escherichia coli DNA polymerase I, and 0.1 unit of Escherichia coli DNase H and the resulting solution was allowed to react at 12°C for one hour and then at 22°C for one hour.

Next, the cDNA-synthesis reaction solution was used to transform *Escherichia coli* DH12S (GIBCO-BRL). The transformation was carried out by the electroporation method. A portion of the transformant was inoculated on a 2xYT agar culture medium containing 100 µg/ml ampicillin, which was

21

incubated at 37°C overnight. A colony grown on the culture medium was randomly picked up and inoculated on 2 ml of the 2xYT culture medium containing 100 µg/ml ampicillin, which was incubated at 37°C overnight. The culture medium was centrifuged 5 to separate the cells, from which a plasmid DNA was prepared by the alkaline lysis method. After the plasmid DNA was doubledigested with EcoRI and NotI, the product was subjected to 0.8% agarose gel electrophoresis to determine the size of the cDNA insert. In addition, by the use of the obtained plasmid as a 10 template, the sequence reaction using M13 universal primer labeled with a fluorescent dye and Taq polymerase (a kit of Applied Biosystems Inc.) was carried out and the product was analyzed by a fluorescent DNA-sequencer (Applied Biosystems Inc.) to determine the base sequence of the cDNA 5'-terminal of 15 about 400 bp. The sequence data were filed as a homo-protein cDNA bank data base.

(3) Selection of cDNAs Encoding Proteins Having
Transmembrane Domains

The base sequence registered in the homo-protein cDNA bank

20 data base was converted to three frames of amino acid sequences
and the presence or absence of an open reading frame (ORF)
beginning from the initiation codon. Then, the selection was
made for the presence of a signal sequence that is
characteristic to a secretory protein at the N-terminal of the

25 portion encoded by ORF. These clones were sequenced from the
both 5' and 3' directions by using the deletion method to
determine the sequence of the whole base sequence. The
hydrophobicity/hydrophilicity profiles were obtained for
proteins encoded by ORF by the Kyte-Doolittle method [Kyte, J.

WO 98/55508

22

PCT/JP98/02445

examine the presence or absence of a hydrophobic region. In the case in which there is a hydrophobic region of putative transmembrane domain(s) in the amino acid sequence of an encoded protein, this protein was considered as a membrane protein.

(4) Construction of Secretory Signal Detection Vector pSSD3

One microgram of pSSD1 carrying the SV40 promoter and a cDNA encoding the protease domain of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)] was digested with 5 units of BglII and 5 units of EcoRV. Then, after dephosphorylation at the 5' terminal by the CIP treatment, a DNA fragment of about 4.2 kbp was purified by cutting off from the gel of agarose gel electrophoresis.

Two oligo DNA linkers, L1 (5'-GATCCCGGGTCACGTGGGAT-3') and L2(5'-ATCCCACGTGACCCGG-3'), were synthesized and phosphorylated by T4 polynucleotide kinase. After annealing of the both linkers, followed by ligation with the previously-20 prepared pSSD1 fragment by T4 DNA ligase, Escherichia coli JM109 was transformed. A plasmid pSSD3 was prepared from the transformant and the objective recombinant was confirmed by the determination of the base sequence of the linker-inserted fragment. Figure 1 illustrates the structure of the thus-25 obtained plasmid. The present plasmid vector carries three types of blunt-end formation restriction enzyme sites, Smal, PmaCI, and EcoRV. Since these cleavage sites are positioned in succession at an interval of 7 bp, selection of an appropriate site in combination of three types of frames for the inserting

23

cDNA allows to construct a vector expressing a fusion protein.

(5) Functional Verification of Secretory Signal Sequence Whether the N-terminal hydrophobic region in the secretory protein clone candidate obtained in the above-mentioned steps functions as the secretory signal sequence was verified by the method described in the literature [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 (1995)]. First, the plasmid containing the target cDNA was cleaved at an appropriate restriction enzyme site that existed at the downstream of the portion 10 expected for encoding the secretory signal sequence. In the case in which this restriction enzyme site was a protruding terminus, the site was blunt-ended by the Klenow treatment or treatment with the mung-bean nuclease. Digestion with HindIII was further carried out and a DNA fragment containing the SV40 15 promoter and a cDNA encoding the secretory sequence at the downstream of the promoter was separated by agarose gel electrophoresis. This fragment was inserted between the pSSD3 HindIII site and a restriction enzyme site selected so as to match with the urokinase-coding frame, thereby constructing a 20 vector expressing a fusion protein of the secretory signal portion of the target cDNA and the urokinase protease domain.

After Escherichia coli (host: JM109) bearing the fusion-protein expression vector was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100 μ g/ml ampicillin, the helper phage M13K07 (50 μ l) was added and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100 μ l of 1 mM Tris-0.1 mM

25

24

EDTA, pH 8 (TE). Also, there was used as a control a suspension of single-stranded particles prepared in the same manner from the vector pLA1-UPA containing pSSD3 and a full-length cDNA of urokinase [Yokoyama-Kobayashi, M. et al., Gene 163: 193-196 5 (1995)].

The simian-kidney-origin culture cells, COS7, incubated at 37°C in the presence of 5% CO2 in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% bovine fetus albumin. Into a 6-well plate (Nunc Inc., 3 cm in the well 10 diameter) were inoculated 1×10^5 COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO2. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) 15 (TDMEM). To the cells were added 1 μ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3 µl of TRANSFECTAMTM (IBF Inc.) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO2. After the sample solution was removed, the cell surface was washed 20 with TDMEM, 2 ml per well of DMEM containing 10% bovine fetus albumin was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO2.

To 10 ml of 50 mM phosphate buffer solution (pH 7.4) containing 2% bovine fibrinogen (Miles Inc.), 0.5% agarose, and 1 mM potassium chloride were added 10 units of human thrombin (Mochida Pharmaceutical Co., Ltd.) and the resulting mixture was solidified in a plate of 9 cm in diameter to prepare a fibrin plate. Ten microliters of the culture supernatant of the

25

transfected COS7 cells were spotted on the fibrin plate, which was incubated at 37°C for 15 hours. The diameter of the thusobtained clear circle was taken as an index for the urokinase activity. In the case in which a cDNA fragment codes for the
5 amino acid sequence that functions as a secretory signal sequence, a fusion protein is secreted to form a clear circle by its urokinase activity. Therefore, in the case in which a clear circle is not formed, the fusion protein remains as trapped in the membrane and the cDNA fragment is considered to
10 code for a transmembrane domain.

(6) Protein Synthesis by In Vitro Translation

The plasmid vector carrying the cDNA of the present invention was utilized for the transcription/translation by the T_NT rabbit reticulocyte lysate kit (Promega Biotec). In this 15 case, $[^{35}S]$ methionine was added and the expression product was labeled with the radioisotope. All reactions were carried out by following the protocols attached to the kit. Two micrograms of the plasmid was allowed to react at 30°C for 90 minutes in total 25 ml of a reaction solution containing 12.5 µl of the TNT rabbit reticulocyte lysate, 0.5 µl of the buffer solution (attached to the kit), 2 µl of an amino acid mixture (methionine-free), 2 μ l (0.37 MBq/ μ l) of [35 S]methionine (Amersham Corporation), 0.5 µl of T7 RNA polymerase, and 20 U of RNasin. To 3 μ l of the reaction solution was added 2 μ l of an SDS sampling buffer (125 mM Tris-hydrochloric acid suffer solution, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting solution was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of

26

the translation product was determined by carrying out the autoradiography.

(7) Expression in COS7

Escherichia coli bearing a vector expressing the protein of the invention was infected with helper phage M13KO7, and single-stranded phage particles were obtained according to the method as stated above. Using the thus obtained phages, each expression vecotr was introduced into simian-kidney-origin culture cells COS7 in the manner as stated above. After incubation at 37 °C for 2 days in the presence of 5 % CO₂, further incubation was carried out in a medium containing [35S]cysteine or [35S]methionine for 1 hour. The cells were collected, dissolved and then subjected to SDS-PAGE whereby a band corresponding to the expression product of each protein which is not present in COS7 cells was revealed. In Table 3, the molecular weight of each expression product is shown.

Table 3

0	HP Number	Supernatant of culture	Membrane fraction
	499.50	(kDa)	(kDa)
	HP01263	50	-
	HP01299	-	30
	HP01526	-	22
5	HP10230	-	24
	HP10408		7
	HP10415	-	45
	HP10424		14
	HP10429	-	27
0	HP10432	-	17
	HP10480	<u>-</u>	22

27

(8) Clone Examples

<HP01263> (Sequence Number 1, 19, 37)

Determination of the whole base sequence for the cDNA insert of clone HP01263 obtained from the human liver cDNA 5 libraries revealed the structure consisting of a 5'-nontranslation region of 36 bp, an ORF of 1149 bp, and a 3'-nontranslation region of 316 bp. The ORF codes for a protein consisting of 382 amino acid residues with one transmembrane domain at the N-terminal. Figure 2 depicts the hydrophobicity 10 /hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in formation of a translation product of 42 kDa, which is almost consistent with the molecular weight of 42,054 as predicted from the ORF. On expression in COS cells, an expression 15 product of about 50 kDa was observed in the culture supernatant. Therefore, said protein can be understood to be a secreted protein. Application of the rule (-3, -1) as a method for anticipation of a cutting site in a secretion signal sequence suggested that the mature protein would start from 20 methionine at 19 position.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human α -2-HS-glycoprotein (SWISS-PROT Accession No. P02765). Table 4 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human α -2-HS-glycoprotein (GP). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the

protein of the present invention. The both proteins possessed a homology of 25.5%. The cysteine position is reserved and this region is analogous to that in cystatins (thiol proteinase inhibitors). There are observed other analogy with histidine-rich glycoprotein (P04196, 30.9%/194 amino acid residues), kininogen (P01045, 24.1%/261 amino acid residues), tyrosine kinase inhibitor (A32827, 24.4%/291 amino acid residues), and so on.

Table 4

10 HP MGLLLPLALCILVLCCGAMSPPQLALNPSALLSR--GCNDSDVLAVAGFALRDINKDRKD .*.** . * . ..*. * .*.*... ..* *. **.. MKSLVLLLCLAQLWGCHSAPHGPGLIYRQPNCDDPETEEAALVAIDYINQNLPW HP GYVLRLNRVNDAQEYRRGGLGSLFYLTLDVLETDCHVLRKKAWQDCGMRIFFE-SVYGQC 15 GP GYKHTLNQIDEVKVWPQQPSGELFEIEIDTLETTCHVLDPTPVARCSVRQLKEHAVEGDC HP K-AIFYMNNPSRVLYLAAYNCTLRPVSKKKIYMTCPDCPSSIPTDSSNHQVLEAATESLA GP DFQLLKLDGKFSVVY---AKCDSSPDSAEDVRKVCQDCPLLAPLN--DTRVVHAAKAALA 20 HP KYNNENTSKQYSLFKVTRASSQWVVGPSYFVEYLIKESPC---TKSQASSCSLQSSDSVP .*..*. * ...** . ** .**. * . ..*..*.. GP AFNAQNNGSNFQLEEISRAQLV-PLPPSTYVEFTVSGTDCVAKEATEAAKCNLLAEKQY-HP VGLCKGSLTRTHWEKFVSVTCDFFESQAPATGSENSAVNQK-PTNLPKVEESQQKNTPPT 25 GP -GFCKATLSEKLGGAEVAVTCTVFQTQPVTSQPQPEGANEAVPTPVVDPDAPPSPPLGAP HP DSPSKAGPRGSVQYLPDLDDKNSQEKGPQEAFPVHLDLTTNPQGETLDISFLFLEPMEEK . *. ..*..* *. GP GLPPAGSPPDSHVLLAAPPGHQLHRAHYDLRHTFMGVVSLGSPSGEVSHPRKTRTVVQPS HP LVVLPFPKEKARTAECPGPAQNASPLVLPP 30 GP VGAAAGPVVPPCPGRIRHFKV

WO 98/55508

10

29

PCT/JP98/02445

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H57204), but it can not be assessed whether these ESTs with 5 partial sequences code for the same protein as the protein of the present invention. Hereupon, most of ESTs matching with the present cDNA are available from liver cDNA libraries, whereby the present clone is considered to be expressed specifically in the liver.

The present protein, because of being a type-II membrane protein, is considered to exert its function as a receptor on the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. The present protein, because of bearing 15 a cystatin-like domain, is considered to possess a proteinaseinhibitor activity as well as many physiological activities in the same manner as for other members of this family. In addition, the present protein, because of being expressed specifically in liver cells, is considered to play a 20 significant role for maintaining the liver function.

<HP01299> (Sequence Number 2, 20, 38)

Determination of the whole base sequence for the cDNA insert of clone HP01299 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-25 translation region of 110 bp, an ORF of 954 bp, and a 3'-nontranslation region of 285 bp. The ORF codes for a protein consisting of 317 amino acid residues with two or more transmembrane domains. 3 Figure depicts the hydrophobicity/hydrophilicity profile of the present protein

30

obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 32 kDa that was almost consistent with the molecular weight of 35,965 predicted from the ORF.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the rat retinol dehydrogenase (NBRF Accession No. A55884). Table 5 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the rat retinol dehydrogenase (RN). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and. represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 65.3% among the entire regions.

Table 5

HP MWLYLAAFVGLYYLLHWYRERQVVSHLQDKYVFITGCDSGFGNLLARQLDARGLRVLAAC 5 RN MWLYLLALVGLWNLLRLFRERKVVSHLQDKYVFITGCDSGFGNLLARQLDRRGMRVLAAC HP LTEKGAEQLRGQTSDRLETVTLDVTKMESIAAATQWVKEHVGDRGLWGLVNNAGILTPIT RN LTEKGAEQLRSKTSDRLETVILDVTKTESIVAATQWVKERVGNRGLWGLVNNAGISVPVG 10 HP LCEWLNTEDSMNMLKVNLIGVIQVTLSMLPLVRRARGRIVNVSSILGRVAFFVGGYCVSK RN PNEWMRKKDFASVLDVNLLGVIEVTLNMLPLVRKARGRVVNIASTMGRMSLVGGGYCISK HP YGVEAFSDILRREIQHFGVKISIVEPGYFRTGMTNMTQSLERMKQSWKEAPKHIKETYGQ 15 RN YGVEAFSDSLRRELTYFGVKVAIIEPGGFKTNVTNMERLSDNLKKLWDQTTEEVKEIYGE HP QYFDALYNIMKEGLLNCSTNLNLVTDCMEHALTSVHPRTRYSAGWDAKFPFIPLSYLPTS RN KFQDSYMKAMESLVNTCSGDLSLVTDCMEHALTSCHPRTRYSPGWDAKFFYLPMSYLPTF HP LADYILTRSWPKPAQAV 20 *.* ***.*. RN LSDAVIHWGSVKPARAL

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. R35197), but any of them was shorter than the present cDNA and did not contain the initiation codon.

The rat retinol dehydrogenase has been found as a microsomal membrane protein participating in the retinoic acid

32

biosynthesis in the liver [Chai, X. et al., J. Biol. Chem. 270: 28408-28412 (1995)]. Accordingly, its homologue, the protein of the present invention, is considered to possess a similar function and can be utilized for diagnosis and treatment of diseases caused by the abnormality of this protein.

<HP01347> (Sequence Number 3, 21, 39)

Determination of the whole base sequence for the cDNA insert of clone HP01347 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-non-10 translation region of 24 bp, an ORF of 891 bp, and a 3'-nontranslation region of 728 bp. The ORF codes for a protein consisting of 296 amino acid residues with one transmembrane domain at the N-terminal. Figure depicts hydrophobicity/hydrophilicity profile of the present protein 15 obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified and the urokinase activity was detected on the membrane surface, upon transduction into the COS7 cells of an expression vector 20 in which a HindIII-SacI fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 73 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein is considered to be a type-II membrane protein. The in vitro 25 translation resulted in the formation of a translation product of 33 kDa that was almost consistent with the molecular weight of 33,527 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was

33

analogous to the human HIV envelope glycoprotein gp120-binding C-type lectin (GenBank Accession No. M98457). Table 6 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human HIV envelope glycoprotein gp120-binding C-type lectin (CL). represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 85.6% among 284 amino acid residues. There is observed at the downstream of the transmembrane domain a sequence with seven repetition of Ile-Tyr-Gln-Xaa-Leu-Thr-Xaa-Leu-Lys-Ala-Ala-Val-Gly-Glu-Leu-Xaa-Xaa-Xaa-Ser-Lys-Xaa-Gln-Xaa.

15

Table 6

	HP	MSDSKEPRVQQLGLLGCLGHGALVLQLLSFMLLAGVLVAI
		******** ****** ****
5	CL	MSDSKEPRLQQLGLLEEEQLRGLGFRQTRGYKSLAGCLGHGPLVLQLLSFTLLAGL
	HP	LVQVSKVPSSLSQEQSEQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE

	CL	LVQVSKVPSSISQEQSRQDAIYQNLTQLKAAVGELSEKSKLQEIYQELTQLKAAVGELPE
	HP	KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTRL
10		********************************
	CL	KSKLQEIYQELTRLKAAVGELPEKSKLQEIYQELTWLKAAVGELPEKSKMQEIYQELTRL
	HP	KAAVGELPEKSKLQEIYQELTELKAAVGELPEKSKLQEIYQELTQLKAAVGELPDQSKQQ
		******* ****** ******* ****************
	CL	KAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQEIYQELTRLKAAVGELPEKSKQQ
15	HP	QIYQELTDLKTAFERLCRHCPKDWTFFQGNCYFMSNSQRNWHDSVTACQEVRAQLVVIKT

	CL	EIYQELTQLKAAVERLCHPCPWEWTFFQGNCYFMSNSQRNWHDSITACKEVGAQLVVIKS
	HP	AEEQLPAVLEQWRTQQ
		**** *. *
20	CL	AEEQNFLQLQSSRSNRFTWMGLSDLNQEGTWQWVDGSPLLPSFKQYWNRGEPNNVGEEDC

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H90360), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The present protein, because of being a type-II membrane 30 protein, is considered to exert its function as a receptor on

the membrane surface with the C-terminal side exposed outside the cells or after undergoing a processing followed by being excreted in the serum. Hereupon, the human HIV envelope glycoprotein gp120-binding C-type lectin that is highly homologous with the present protein has been found as a CD4-independent HIV receptor [Curtis, B. M. et al., Proc. Natl. Acad. Sci. USA 89: 8356-8360 (1992)].

<HP01440> (Sequence Number 4, 22, 40)

insert of clone HP01440 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 37 bp, an ORF of 594 bp, and a 3'-non-translation region of 98 bp. The ORF codes for a protein consisting of 197 amino acid residues with four transmembrane domains. Figure 5 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 20,822 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the human tumor-associated antigen L6 (SWISS-PROT Accession No. P30408). Table 7 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the human tumor-associated antigen L6 (L6).

- represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed

36

a homology of 47.0% among the entire regions.

Table 7

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. T55097), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

The human tumor-associated antigen L6 is a member of a membrane antigen TM4 superfamily proteins which are expressed in large quantities on the surface of human tumor cells [Marken, J. S. et al., Proc. Natl. Acad. Sci. USA 89: 3503-3507 (1992)]. Since these membrane antigens are expressed specifically on some specified cells or cancer cells,

20

37

PCT/JP98/02445

antibodies against these antigens, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are 5 expressed are applicable for detection of the corresponding ligands and so on.

<HP01526> (Sequence Number 5, 23, 41)

Determination of the whole base sequence for the cDNA insert of clone HP01526 obtained from the human stomach cancer 10 cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 83 bp, an ORF of 666 bp, and a 3'-nontranslation region of 573 bp. The ORF codes for a protein consisting of 221 amino acid residues with a hydrophobic region of putative six transmembrane domains. Figure 6 depicts the 15 hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was almost consistent with the molecular weight of 25,030 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the mouse interstitial cell protein (GenBank Accession No. X96618). Table 8 indicates the comparison of the amino acid sequences between the human protein of the present 25 invention (HP) and the mouse interstitial cell protein (MM). represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed 38

a homology of 79.6% among the entire regions.

Table 8

Furthermore, the search of GenBank using the base sequence 20 of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. H02682), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

25 The mouse interstitial cell protein has been cloned as a membrane protein that is expressed with highly increasing in interstitial cells stimulated by a cytokine [Tagoh, H. et al., Biochem. Biophys. Res. Commun. 221: 744-749 (1996)]. Since these membrane proteins are expressed specifically on some 30 specified cells and cancer cells, antibodies against these

proteins, if constructed, are useful for a variety of diagnoses and as carriers for the drug delivery. In addition, the cells in which genes of these membrane antigens are transduced and the membrane antigens are expressed are applicable for 5 detection of the corresponding ligands and so on.

39

PCT/JP98/02445

<HP10230> (Sequence Number 6, 24, 42)

Determination of the whole base sequence for the cDNA insert of clone HP10230 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-10 translation region of 190 bp, an ORF of 756 bp, and a 3'-nontranslation region of 2099 bp. The ORF codes for a protein consisting of 251 amino acid residues with at least one transmembrane domain. Figure depicts hydrophobicity/hydrophilicity profile of the present protein 15 obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 30 kDa that was almost consistent with the molecular weight of 28,800 predicted from the ORF.

The search of the protein data base using the amino acid 20 sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein F25D7.1 (GenBank Accession No. 278418). Table 9 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein F25D7.1 25 (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 49.8% among the entire regions.

Table 9

- HS MSDIGDWFRSIPAITRYWFAATVAVPLVGKLGLISPAYLFL-WPEAFLYRFQIWRPITAT 5 CE MDLENFLLGIPIVTRYWFLASTIIPLLGRFGFINVQWMPLQW-DLVVNKFQFWRPLTAL HS FYFPVGPGTGFLYLVNLYFLYQYSTRLETGAFDGRPADYLFMLLFNW-ICIVITGLAMDM CE IYYPVTPQTGFHWLMMCYFLYNYSKALESETYRGRSADYLFMLIFNWFFCSGLC-MALDI HS QLLMIPLIMSVLYVWAQLNRDMIVSFWFGTRFKACYLPWVILGFNYIIGGSVINELIGNL .*. *...***** *.*.* ****** ** * *****. *** .. *. .***.* * 10 CE YFLLEPMVISVLYVWCQVNKDTIVSFWFGMRFPARYLPWVLWGFNAVLRGGGTNELVGIL HS VGHLYFFLMFRYPMDLGGRNFLSTPQFLYRWLPSRRGGVSGFGVPPASMRRAADQNGGGG *** ***. ..** . * ...**.*.* .*. **. * CE VGHAYFFVALKYPDEYGV-DLISTPEFLHRLIPDEDGGIHG---QDGNIRGARQQPRG--15 HS RHNW--GQGFRLGDQ CE -HQWPGGVGARLGGN
- 20 Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more and also containing the initiation codon (for example, Accession No. W01493), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10389> (Sequence Number 7, 25, 43)

Determination of the whole base sequence for the cDNA insert of clone HP10389 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure consisting of a 5'-non-translation region of 62 bp, an ORF of

10

41

PCT/JP98/02445

321 bp, and a 3'-non-translation region of 270 bp. The ORF codes for a protein consisting of 106 amino acid residues with a hydrophobic region of putative two transmembrane domains. Figure 8 depicts the hydrophobicity/hydrophilicity profile of 5 the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 12 kDa that was almost consistent with the molecular weight of 11,528 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any of known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. H70816), but many sequences 15 were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10408> (Sequence Number 8, 26, 44)

Determination of the whole base sequence for the cDNA insert of clone HP10408 obtained from the human stomach cancer 20 cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 74 bp, an ORF of 237 bp, and a 3'-nontranslation region of 128 bp. The ORF codes for a protein consisting of 78 amino acid residues with a putative signal sequence at the N-terminal as well as a sequence of one 25 putative interior transmembrane domain. Figure 9 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified

upon transduction into the COS7 cells of an expression vector in which a HindIII-BglII fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 70 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 9 kDa that was almost consistent with the molecular weight of 8,396 predicted from the ORF.

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T94049), but they were shorter than the present cDNA and any molecule containing the initiation codon was not identified.

15 <HP10412> (Sequence Number 9, 27, 45)

Determination of the whole base sequence for the cDNA insert of clone HP10412 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 55 bp, an ORF of 945 bp, and a 3'-non-20 translation region of 131 bp. The ORF codes for a protein consisting of 314 amino acid residues with one transmembrane N-terminal. Figure 10 depicts the domain at the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that 25 the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-ApaI fragment (treated with mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 65

43

amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. The in vitro translation resulted in the formation of a translation product of 44 kDa that was somewhat larger than the molecular weight of 35,610 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the nematode hypothetical protein of 28.5 kDa (SWISS-PROT Accession No. P34623). Table 10 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the nematode hypothetical protein of 28.5 kDa (CE). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 42.8% in the C-terminal region of 243 amino acid residues.

Table 10

HP MVAPVWYLVAAALLVGFILFLTRSRGRAASAGQEPLHNEELAGAGRVAQPGPLEPEEPRA 5 HP GGRPRRRDLGSRLQAQRRAQRVAWAEA--DENEEEAVILAQEEEGVEKPAETHLSGKIG CE MRRNARRRVNRDEQEDGFVNHMMNDGEDVEDLDGGAEQFEYDEDGKKIG HP AKKLRKLEEKQARKAQREAEEAEREERKRLESQREAEWKKEEERLRLEEEQKEEEE--RK .* **..*... ** * ****** *..* * *..** . *...*.** 10 CE KRKAAKLQAKEEKRQMREYEVREREERKRREEER.-EKKRDEERAKERADEKAEEERLRK HP AREEQAQREHEEYLKLKEAFVVEEEGVGETMTEEQSQSFLTEFINYIKQSKVVLLEDLAS CE EREEKERKEHEEYLAMKASFAIEEEG-TDAIEGEEAENLIRDFVDYVKTNKVVNIDELSS HP QVGLRTQDTINRIQDLLAEGTITGVIDDRGKFIYITPEELAAVANFIRQRGRVSIAELAQ 15 . **...*..**.* . **.******* . **.****** *.*. CE HFGLKSEDAVNRLQHFIEEGLVQGVMDDRGKFIYISDEEFAAVAKFINQRGRVSIHEIAE HP ASNSLIAWGRESPAQAPA .**.** . *.*. CE QSNRLIRLETPSAAE 20

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T09311), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10413> (Sequence Number 10, 28, 46)

Determination of the whole base sequence for the cDNA 30 insert of clone HP10413 obtained from the human stomach cancer

45

cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 78 bp, an ORF of 588 bp, and a 3'-nontranslation region of 1209 bp. The ORF codes for a protein consisting of 195 amino acid residues with one transmembrane N-terminal. the Figure 11 depicts hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-PmaCI fragment containing a cDNA fragment encoding the N-terminal 65 amino acid residues in the present protein was inserted at the HindIII-PmaCI site of pSSD3. The in vitro translation resulted in the formation of a translation 15 product of 28 kDa that was somewhat larger than the molecular weight of 21,671 predicted from the ORF.

10

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the swine steroidal membrane-binding protein 20 (GenBank Accession No. X99714). Table 11 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the swine steroidal membrane-binding protein (SS). - represents a gap, * represents an amino acid residue identical to that in the protein of the 25 present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 96.4% among the entire regions.

46

Table 11

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA021062), but many sequences were not distinct and the same ORF as that in the present cDNA was not identified.

<HP10415> (Sequence Number 11, 29, 47)

Determination of the whole base sequence for the cDNA insert of clone HP10415 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-non-translation region of 71 bp, an ORF of 1389 bp, and a 3'-non-translation region of 103 bp. The ORF codes for a protein consisting of 462 amino acid residues with one transmembrane domain at the N-terminal. Figure 12 depicts the hydrophobicity/hydrophilicity profile of the present protein

47

obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 48 kDa that was somewhat smaller than the molecular weight of 52,458 predicted from the ORF.

5

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the cytochrome P450 as exemplified by the simian cytochrome P450IIIA8 (SWISS-PROT Accession No. P33268). Table 12 indicates the comparison of the amino acid sequences between 10 the human protein of the present invention (HP) and the simian cytochrome P450IIIA8 (CP). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The 15 both proteins possessed a homology of 21.3% among the entire regions.

48

Table 12

	HP	MLDFAIFAVTFLLALVGAVLYLYPASRQAAGIPGITPTEEKDGNLPDIVN-SGSLHEF
		.****
5	CP	${\tt MDLIPDLAVETWLLLAVTLVLLYLYGTHSHGLFKKLGIPGPTPLPLLGNILSYRKGFWTF}$
	HP	LVNLHERYGPVVSFWFGRRLVVSLGTVDVLKQHINPNKTLDPFETMLK-SLLRYQSGGGS
		** * .*. **. *
	CP	DMECYKKYGKVWGFYDGRQPVLAITDPNMIK-TVLVKECYSVFTNRRPFGPVGFMKNAIS
	HP	VSENHMRKKLYENGVTDSLKSNFALLLKLSEKLLDKWLSYPET-QHVPLSQHMLGF
10		**. *** * ***
	CP	IAEDEEWKRIRSLLSPTFTSGKLKEMVPIIAKYGDVLVRNLRREAETGKPVTLKDVFGAY
	HP	AMKSVTQMVMGSTF-EDDQEVIRFQKNHGTVWSEIGKGFLDGSLDKNM
		.** .* * *. * *
	CP	${\tt SMDVITSTSFGVNIDSLNNPQDPFVENTKKLLRFDFLDPFFLSITIFPFIIPILEVLNIS}$
15	HP	TRKKQYEDALMQ-LESVLRNIIKE-RKGR-NFSQHIFIDSLVQGNLNDQQILEDS
		*
	CP	IFPREVTSFLRKSVKRIKESRLKDTQKHRVDFLQLMIDSQNSKETESHKALSDLELVAQS
	HP	MIFSLASCIITAKLCTWAICFLTTSEEVQKKLYEEINQVF-GNGPVTPEKIEQLRYCQHV
		.** .** *. ***. **. * * * . *
20	CP	IIFIFAGYETTSSVLSFIIYELATHPDVQQKLQEEIDTVLPNKAPPTYDTVLQMEYLDMV
	HP	LCETVRTAKLTPVSAQLQDIEGKIDRFIIPRETLVLYALGVVLQDPNTWPSPHKFDPDRF
		. **.*****
	HP	VNETLRIFPIAMRLERVCKKDVEINGIFIPKGVVVMIPSYALHHDPKYWPEPEKFLPERF
	HP	DDELVMKTFSSLGFSGTQECPELRFAYMVTTVLLSVLVKRLHLLSVEGQVIETKYE
25		.* ** * *
	CP	SKKNNDNIDPYTYTPFG-SGPRNCIGMRFALMNMKLATIRVLQNFSFKPCKETQIPLKLR
	HP	LVTSSREEAWITVSKRY
		*
	CP	LGGLLQTEKPIVLKIESRDGTVSGA
20		

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs

PCT/JP98/02445 WO 98/55508

possessing the homology of 90% or more (for example, Accession No. AA381169), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

The cytochrome P450 participates in the drug metabolism · 5 and can be utilized as a catalyst in organic synthesis reactions such as oxidation and so on.

<HP10419> (Sequence Number 12, 30, 48)

10

Determination of the whole base sequence for the cDNA insert of clone HP10419 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 170 bp, an ORF of 744 bp, and a 3'-nontranslation region of 1116 bp. The ORF codes for a protein consisting of 247 amino acid residues with a hydrophobic region 15 of putative seven transmembrane domains. Figure 13 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

The search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing 20 the homology of 90% or more (for example, Accession No. AA340663), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10424> (Sequence Number 13, 31, 49)

25 Determination of the whole base sequence for the cDNA insert of clone HP10424 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 97 bp, an ORF of 342 bp, and a 3'-nontranslation region of 54 bp. The ORF codes for a protein

50

consisting of 113 amino acid residues with one transmembrane N-terminal. Figure 14 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified upon transduction into the COS7 cells of an expression vector in which a HindIII-AccI fragment (after the Klenow treatment) containing a cDNA fragment encoding the N-terminal 58 amino 10 acid residues in the present protein was inserted at the HindIII-SmaI site of pSSD3. The in vitro translation resulted in the formation of a translation product of 14 kDa that was somewhat larger than the molecular weight of 12,784 predicted from the ORF.

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA401979), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein 20 of the present invention.

<HP10428> (Sequence Number 14, 32, 50)

15

Determination of the whole base sequence for the cDNA insert of clone HP10428 obtained from the human epidermoid carcinoma cell line KBc cDNA libraries revealed the structure 25 consisting of a 5'-non-translation region of 287 bp, an ORF of 1098 bp, and a 3'-non-translation region of 659 bp. The ORF codes for a protein consisting of 365 amino acid residues with a hydrophobic region of putative nine transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile of

51

the present protein obtained by the Kyte-Doolittle method. The result of the in vitro translation did not reveal the formation of distinct bands and only revealed the formation of smeary bands at the high-molecular-weight position.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was analogous to the baker's yeast hypothetical membrane protein YML038c (NBRF Accession No. 549741). Table 13 indicates the comparison of the amino acid sequences between the human protein of the present invention (HP) and the baker's yeast hypothetical membrane protein YML038c (SC). - represents a gap, * represents an amino acid residue identical to that in the protein of the present invention, and . represents an amino acid residue analogous to that in the protein of the present invention. The both proteins possessed a homology of 26.3% among the N-terminal region of 281 amino acid residues.

52

Table 13

	_	
	HP	MGRWALDVAFLWKAVLTLGLVL-LYYCFSIGITFYNKWLTKSFHFPLFMTMLHLA
		**. *.* **
5	sc	MNRTVFLAFVFGWYFCS-IALSIYNRWMFDPKDGLGIGYPVLVTTFHQA
	HP	VIFLFSALSRALVQCSSHRARVVLSWADYLRRVAPTALATALDVGLSNWSFLYVTVS
		****** ** ***
	sc	TLWLLSGIYIKLRHKPVKNVLRKNNGFNWSFFLKFLLPTAVASAGDIGLSNVSFQYVPLT
	HP	Lytmtkssavlfilifslifkleelraalvlvvlliagglfmftykstq-fn
10		.**** *.*.*
	sc	IYTIIKSSSIAFVLLFGCIFKLEKFHWKLALSVIIMFVGVALMVFKPSDSTSTKNDQALV
	HP	VEGFALVLGASFIGGIRWTLTQMLLQKAELGLQNPIDTMFHLQPLMFLGLFPLFAVFEGL
		. * *****.**. ***
	sc	IFGSFLVLASSCLSGLRWVYTQLMLRNNPIQTNTAAAVEES-DGALFTENEDNVDNEPVV
15	HP	HLSTSEKIFRFQDT-GLLLRVLGSLFLGGILAFGLGFSEFLLVSRTSSLTLSIAGIFKEV
		.* * * *. * * *** ***.
	sc	NLANNKMLENFGESKPHPIHTIHQLAPIMGITLLLTS-LLVEKPFPGIFS-SSIFRLD
	HP	CTLLLAAHLLGDQISLLNWLGFALCLSGISLHVALKALHSRGDGGPKALKGLGSSPDLEL
20	sc	TSNGGVGTETTVLSIVRGIVLLILPGFAVFLLTICEFSILEQTPVLTVSIVGIVKELLTV
	HP	LLRSSQREEGDNEEEEYFVAQGQQ
	sc	IFGIIILSERLSGFYNWLGMLIIMADVCYYNYFRYKQDLLQKYHSVSTQDNRNELKGFQD

25

Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. AA018345), but it can not be assessed whether these ESTs

15

WO 98/55508 PCT/JP98/02445

53

with partial sequences code for the same protein as the protein of the present invention.

<HP10429> (Sequence Number 15, 33, 51)

Determination of the whole base sequence for the cDNA 5 insert of clone HP10429 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 156 bp, an ORF of 681 bp, and a 3'-nontranslation region of 206 bp. The ORF codes for a protein consisting of 226 amino acid residues with four transmembrane 10 domains. Figure 16 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 25 kDa that was almost consistent with the molecular weight of 25,321 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or 20 more (for example, Accession No. AA315933), but it can not be assessed whether these ESTs with partial sequences code for the same protein as the protein of the present invention.

<HP10432> (Sequence Number 16, 34, 52)

Determination of the whole base sequence for the cDNA insert of clone HP10429 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 28 bp, an ORF of 390 bp, and a 3'-nontranslation region of 554 bp. The ORF codes for a protein consisting of 129 amino acid residues with a signal-like

sequence at the N-terminal and one interior transmembrane domain. Therefore, the present protein is considered to be a type-I membrane protein. Figure 17 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method.

54

PCT/JP98/02445

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or more (for example, Accession No. T74424), but the same ORF as that in the present cDNA was not identified.

<HP10433> (Sequence Number 17, 35, 53)

Determination of the whole base sequence for the cDNA insert of clone HP10433 obtained from the human liver cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 72 bp, an ORF of 492 bp, and a 3'-nontranslation region of 131 bp. The ORF codes for a protein consisting of 163 amino acid residues with one transmembrane 20 domain at the N-terminal. Figure 18 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. It was indicated that the present protein remained in the membrane from the observation that the urokinase secretion was not identified 25 upon transduction into the COS7 cells of an expression vector in which a HindIII-Eco81I fragment (treated with the mung-bean nuclease) containing a cDNA fragment encoding the N-terminal 137 amino acid residues in the present protein was inserted at the HindIII-EcoRV site of pSSD3. Therefore, the present protein

5

15

PCT/JP98/02445

is considered to be a type-II membrane protein. The in vitro translation resulted in the formation of a translation product of 21 kDa that was almost consistent with the molecular weight of 18,617 predicted from the ORF.

55

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or 10 more (for example, Accession No. H84693), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

<HP10480> (Sequence Number 18, 36, 54)

Determination of the whole base sequence for the cDNA insert of clone HP10480 obtained from the human stomach cancer cDNA libraries revealed the structure consisting of a 5'-nontranslation region of 79 bp, an ORF of 582 bp, and a 3'-nontranslation region of 1253 bp. The ORF codes for a protein consisting of 193 amino acid residues with four transmembrane 20 domains. Figure 19 depicts the hydrophobicity/hydrophilicity profile of the present protein obtained by the Kyte-Doolittle method. The in vitro translation resulted in the formation of a translation product of 23 kDa that was somewhat larger than the molecular weight of 21,445 predicted from the ORF.

25 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was not analogous to any known proteins. Furthermore, the search of GenBank using the base sequence of the present cDNA revealed that there existed some ESTs possessing the homology of 90% or

РСТ/ЈР98/02445

more (for example, Accession No. W93606), but many sequences are not distinct and the same ORF as that in the present cDNA was not identified.

56

The present invention provides human proteins having transmembrane domains and cDNAs encoding said proteins. All of the proteins of the present invention are putative proteins controlling the proliferation and differentiation of the cells, because said proteins exist on the cell membrane. Therefore, the proteins of the present invention can be used as 10 pharmaceuticals or as antigens for preparing antibodies against said proteins. Furthermore, said DNAs can be used for the expression of large amounts of said proteins. The cells expressing large amounts of membrane proteins with transfection of these membrane protein genes can be applied to the detection 15 of the corresponding ligands, the screening of novel low-molecular medicines, and so on.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant protein for

57

analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA 10 sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known in the process of discovering other polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for 15 examination of expression patterns; to raise anti-protein antibodiesusing DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in

assays designed to quantitatively determine levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. Proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of 15 being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source

and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

Cytokine and Cell Proliferation/Differentiation

10 Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1165, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H.

PCT/JP98/02445

Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Bertagnolli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

60

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Po lyclonal T cell stimulation, Kruisbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon γ, Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays proliferation and for differentiation hematopoietic and lymphopoietic cells include, without 20 limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; deVries et al., J. Exp. Med. 173:1205-1211, 25 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6 -Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et

- al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986;
 Measurement of human Interleukin 11 Bennett, F., Giannotti,
 J., Clark, S.C. and Turner, K. J. In Current Protocols in
 Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley
 and Sons, Toronto. 1991; Measurement of mouse and human
 Interleukin 9 Ciarletta, A., Giannotti, J., Clark, S.C. and
 Turner, K.J. In Current Protocols in Immunology. J.B.e.a.
 Coligan eds. Vol 1 pp. 6.13.1, John Wiley and Sons, Toronto.
 1991.
- 10 Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols 15 Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); 20 Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined

62

PCT/JP98/02445

WO 98/55508

immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as effecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial orfungal infections, or may result from autoimmune disorders. More specifically, infectious diseases causes by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, Leishmania spp., malaria spp. and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may

15 Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, 20 insulin dependent diabetes mellitis, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also to be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or 25 other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, transplantation), may also be treatable using a protein of the present invention.

be desirable, i.e., in the treatment of cancer.

Using the proteins of the invention it may also be

63

possible to immune responses, in a number of ways. regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, 10 which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure 15 to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its 25 recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2

64

activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen B7-1, B7-3) or blocking antibody), prior transplantation can lead to the binding of the molecule to the 5 natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as immunosuppressant. Moreover, the lack of costimulation may 10 also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or tolerance in a subject, it may 15 also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

20

25

65

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the 5 production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor: ligand interactions of B lymphocyte 10 antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythmatosis in MRL/lpr/lpr mice or NZB hybrid 20 mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B

66

WO 98/55508

20

lymphocyte antigen function may be useful in cases of viral In addition, systemic viral diseases such as infection. influenza, the commoncold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte 5 antigens systemically.

PCT/JP98/02445

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or 10 together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein 15 of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the transfected cells into the patient. infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least 25 one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression

vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface 10 of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II 15 molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I α chain protein and eta_2 microglobulin protein or an MHC class IIa chain protein and an MHC class IIB chain protein to thereby express MHC class I or MHC class II proteins 20 on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which 25 blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a

PCT/JP98/02445

68

T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

5 Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays 10 for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 15 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowmanet al., J. Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 20 Bertagnolli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that 25 affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John

Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those 5 described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in 10 Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnolli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that 15 activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porgador et al., Journal of Experimental Medicine 20 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965, 1994; Macatonia et al., Journal of Experimental 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of 25 Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in:

70

PCT/JP98/02445

Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamai et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad Sci. USA 88:7548-7551, 1991.

Hematopoiesis Regulating Activity

A protein of the present invention may be useful in 15 regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation 20 of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to stimulate the production of erythroid precursors and/or erythroid cells; in supporting the 25 growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently

WO 98/55508

71

PCT/JP98/02445

of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complimentary to platelet transfusions; and/or in supporting the growth and proliferation 5 of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal 10 nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo ex-vivo conjunction (i.e., in with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells 15 or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney,

M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area cell assay, Ploemacher, R.E. In Culture 10 Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooncer, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., 15 New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

Tissue Growth Activity

- A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.
- A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the

73

invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, 20 which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a 25 tendon/ligament-like tissue inducing protein may prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue

74

formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of 5 tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon- or ligament-forming cells, stimulate growth of tendonligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of 10 tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. compositions may also include an appropriate matrix and/or 15 sequestering agent as a carrier as is well known in the art.

The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as 20 mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized 25 neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders,

WO 98/55508

PCT/JP98/02445

such as spinal cord disorders, head trauma and cerebrovascular diseases such as stroke. Peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

75

- Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.
- It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.
- A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

A protein of the present invention may also be useful for 25 promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

76

Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. W095/16035 (bone, cartilage, tendon); International Patent Publication No. W095/05846 5 neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year 10 Book Medical Publishers, Inc., Chicago, as modified by Eaglstein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

Activin/Inhibin Activity

A protein of the present invention may also exhibit or inhibin-related activities. Inhibins 15 characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of 20 the inhibin α family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals. Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, 25 as a homodimer or as a heterodimer with other protein subunits of the inhibin-β group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of

WO 98/55508

the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

77

PCT/JP98/02445

5 The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., Endocrinology 91:562-572, 1972; Ling et al., Nature 321:779-782, 1986; Vale et al., Nature 321:776-779, 1986; Mason et al., Nature 318:659-663, 1985; Porage et al., Proc. Natl. Acad. Sci. USA 83:3091-3095, 1986.

Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell

78

population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis)consist of assays

10 that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: Current Protocols in

15 Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. J. Clin. Invest. 95:1370-1376, 1995; Lind et al. APMIS 103:140-146, 1995; Muller et al Eur. J. Immunol. 25: 1744-1748; Gruber et al. J. of Immunol. 152:5860-5867, 1994; Johnston et al. J. of Immunol. 153: 1762-1768, 1994.

Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (includinghereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A

WO 98/55508

PCT/JP98/02445

protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system 5 vessels (e.g., stroke).

79

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include, without limitation, those described in: Linet et al., J. Clin.

10 Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res.
45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

Receptor/Ligand Activity

A protein of the present invention may also demonstrate 15 activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors 20 involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their liqunds) and receptor/liqund pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). 25 Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments receptors and ligands) may themselves be useful as inhibitors

80

of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include

5 without limitation those described in:Current Protocols in
Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies,
E.M. Shevach, W.Strober, Pub. Greene Publishing Associates and
Wiley-Interscience (Chapter 7.28, Measurement of Cellular
Adhesion under static conditions 7.28.1-7.28.22), Takai et al.,

10 Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al.,
J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp.
Med. 169:149-160 1989; Stoltenborg et al., J. Immunol.
Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

Anti-Inflammatory Activity

15 Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), 20 inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting orpromoting extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can 25 be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis,

complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of ytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities. A protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

20 Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in

82

bone form or shape); effecting biorhythms or caricadic cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, 5 protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent 10 behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related 15 diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another 20 material or entity which is cross-reactive with such protein.

WO 98/55508

83

Sequence Table

	(2)	INF	ORMA'	поі	FOR	SEQ	ID I	10:	l:							
5		(:	i) SI	QUE	NCE (CHARA	ACTE	RIST	cs:							
				(A)	LENG	HT:	382									
				(B)	TYPI	E: Ai	nino	acio	i							
				(D)	TOP	DLOGY	: L	inear	r							
		(:	li) S	EQUI	ENCE	KIN): P	rote	in							
10		(:	iii)	HYPO	OTHE:	ricai	L: No	5								
		(7	7i) (ORIG	INAL	SOU	RCE:	•								
				(A)	ORGA	ANISI	1: H	omo :	sapi	ens						
				(B)	CELI	L KI	ND: 1	Live	r							
15				(D)	CLO	NE NA	AME:	HPO:	1263							
		(2	ki) S	EQUI	ENCE	DESC	CRIP	rion	SEC) ID	NO:	1:				
•		Gly	Leu	Leu		Pro	Leu	Ala	Leu		Ile	Leu	Val	Leu	Cys	Сув
20	1				5	_		_		10				_	15	_
	GLÀ	Ala	Met		Pro	Pro	Gln	Leu		Leu	Asn	Pro	Ser		Leu	Leu
	Co=	A	C1-	20	4		0		25		43.	1	4.1	30	D1	
	261	vrR	35	cys	Asn	Asp	Set	Asp 40	AST	Leu	ATB	var		ета	Phe	AIA
25	Lou	Ara		Tlo	400	I wo	Ann	-	1	400	C1	T	45	1	Arg	Lou
23	Deu	50	nsp	116	non	Lys	55	nig	ьуѕ	мър	GIY	60	Val	Leu	ALE	Leu
	Asn		Va 1	Asn	Asn	A1a		Glu	Tur	Ara	Ara		G1 w	T.011	G1y	Sar
	65	8				70		014	-,-	••• Б	75	OL,	or,	Bea	01)	80
	Leu	Phe	Tyr	Leu	Thr		Asp	Val	Leu	Glu		Asp	Cvs	His	Val	
30			•		85		•			90			-,-		95	
	Arg	Lys	Lys	Ala	Trp	Gln	Asp	Cys	Gly	Met	Arg	Ile	Phe	Phe	Glu	Ser
				100	-		·		105		J			110		
	Val	Tyr	Gly	Gln	Cys	Lys	Ala	Ile	Phe	Tyr	Met	Asn	Asn	Pro	Ser	Arg
			115					120		-			125			
35	Val	Leu	Tyr	Leu	Ala	Ala	Tyr	Asn	Cys	Thr	Leu	Arg	Pro	Val	Ser	Lys
		130					135					140				
	Lys	Lys	Ile	Tyr	Met	Thr	Cys	Pro	Asp	Cys	Pro	Ser	Ser	Ile	Pro	Thr
	145					150					155					160

	Asp	Ser	Ser	Asn	His	Gln	Val	Leu	Glu	Ala	Ala	Thr	Glu	Ser	Leu	Ala
					165					170					175	
	Lys	Tyr	Asn	Asn	Glu	Asn	Thr	Ser	Lys	Gln	Tyr	Ser	Leu	Phe	Lys	Val
				180					185					190		
5	Thr	Arg	Ala	Ser	Ser	Gln	Trp	Val	Va1	Gly	Pro	Ser	Tyr	Phe	Val	Glu
			195					200					205			
	Tyr	Leu	Ile	Lys	Glu	Ser	Pro	Cys	Thr	Lys	Ser	Gln	Ala	Ser	Ser	Cys
	•	210					215					220				
	Ser	Leu	Gln	Ser	Ser	Asp	Ser	Val	Pro	Val	Gly	Leu	Cys	Lys	Gly	Ser
10	225					230					235					240
	Leu	Thr	Arg	Thr	His	Trp	Glu	Lys	Phe	Val	Ser	Val	Thr	Cys	Asp	Phe
					245					250					255	
	Phe	Glu	Ser	Gln	Ala	Pro	Ala	Thr	Gly	Ser	Glu	Asn	Ser	Ala	Val	Asn
				260					265					270		
15	Gln	Lys	Pro	Thr	Asn	Leu	Pro	Lys	Val	Glu	Glu	Ser	Gln	Gln	Lys	Asn
			275					280					285			
	Thr	Pro	Pro	Thr	Asp	Ser	Pro	Ser	Lys	Ala	Gly	Pro	Arg	Gly	Ser	Val
		290					295					300				
	Gln	Tyr	Leu	Pro	Asp	Leu	Asp	Asp	Lys	Asn	Ser	Gln	Glu	Lys	Gly	Pro
20	305					310					315					320
	Gln	Glu	Ala	Phe		Val	His	Leu	Asp	Leu	Thr	Thr	Asn	Pro	Gln	Gly
					325					330					335	
	Glu	Thr	Leu	Asp	Ile	Ser	Phe	Leu		Leu	Glu	Pro	Met		Glu	Lys
				340					345					350		
25	Leu	Val		Leu	Pro	Phe	Pro		Glu	Lys	Ala	Arg		Ala	Glu	Cys
			355					360					365			
	Pro		Pro	Ala	GIn	Asn		Ser	Pro	Leu	Val		Pro	Pro		
	•	370					375					380				
30																
311																

- (2) INFORMATION FOR SEQ ID NO: 2:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 317
 - (B) TYPE: Amino acid
- -35 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No

85

(vi)	ORIGINAL	SOURCE:
------	----------	---------

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Liver

(D) CLONE NAME: HP01299

5

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

	Met	Trp	Leu	Tvr	Leu	Ala	Ala	Phe	Va1	G1v	Leu	Tvr	Tvr	Leu	Leu	His
	1			-,-	5					10		-,-	-,-		15	
10		Tvr	Are	Glu		Gln	Val	Val	Ser		I.eu	Gln	Asp	Lys		Va 1
		-,-	8	20	6				25					30	-,-	
	Phe	Ile	Thr	Gly	Cys	Asp	Ser	Gly		Gly	Asn	Leu	Leu	Ala	Arg	Gln
			35	•	-	•		40					45			
	Leu	Asp	Ala	Arg	Gly	Leu	Arg	Val	Leu	Ala	Ala	Cys	Leu	Thr	Glu	Lys
15		50			•		55					60				
	Gly	Ala	Glu	Gln	Leu	Arg	Gly	G1n	Thr	Ser	Asp	Arg	Leu	Glu	Thr	Val
	65					70					75					80
	Thr	Leu	Asp	Val	Thr	Lys	Met	Glu	Ser	Ile	Ala	Ala	Ala	Thr	Gln	Trp
					85					90					95	
20	Val	Lys	Glu	His	Val	Gly	Asp	Arg	Gly	Leu	Trp	Gly	Leu	Val	Asn	Asn
				100					105					110		
	Ala	Gly	Ile	Leu	Thr	Pro	Ile	Thr	Leu	Cys	Glu	Trp	Leu	Asn	Thr	Glu
			115					120					125			
	Asp	Ser	Met	Asn	Met	Leu	Lys	Val	Asn	Leu	Ile	Gly	Val	Ile	Gln	Val
25		130					135					140				
	Thr	Leu	Ser	Met	Leu	Pro	Leu	Val	Arg	Arg	Ala	Arg	Gly	Arg	Ile	Val
	145					150					155					160
	Asn	Val	Ser	Ser	Ile	Leu	Gly	Arg	Val	Ala	Phe	Phe	Val	Gly	Gly	Tyr
					165					170					175	
30	Cys	Val	Ser		Tyr	Gly	Val	Glu		Phe	Ser	Asp	Ile	Leu	Arg	Arg
				180					185					190		
	Glu	Ile		His	Phe	Gly	Val	-	Ile	Ser	Ile	Val		Pro	Gly	Tyr
			195					200					205			_
25	Phe		Thr	Gly	Met	Thr		Met	Thr	Gln	Ser		Glu	Arg	Met	Lys
35		210	_				215	_				220		_		
		ser	тrр	Lys	Glu		Pro	Lys	His	Ile	•	Glu	Thr	Tyr	GLY	
	225	m	nı.	A =	4.7	230			~•		235	••	٥.			240
	GIN	Tyr	rne	Asp	Ala	Leu	Tyr	Asn	lle	Met	Lys	Glu	Gly	Leu	Leu	Asn

86 245 250 Cys Ser Thr Asn Leu Asn Leu Val Thr Asp Cys Met Glu His Ala Leu Thr Ser Val His Pro Arg Thr Arg Tyr Ser Ala Gly Trp Asp Ala Lys 5 280 Phe Phe Phe Ile Pro Leu Ser Tyr Leu Pro Thr Ser Leu Ala Asp Tyr 295 300 Ile Leu Thr Arg Ser Trp Pro Lys Pro Ala Gln Ala Val 310 315 10 (2) INFORMATION FOR SEQ ID NO: 3: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 296 15 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Liver (D) CLONE NAME: HP01347 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3: Met Ser Asp Ser Lys Glu Pro Arg Val Gln Gln Leu Gly Leu Leu Gly 1 15 5 10 Cys Leu Gly His Gly Ala Leu Val Leu Gln Leu Leu Ser Phe Met Leu 30 25 Leu Ala Gly Val Leu Val Ala Ile Leu Val Gln Val Ser Lys Val Pro 35 40 45 Ser Ser Leu Ser Gln Glu Gln Ser Glu Gln Asp Ala Ile Tyr Gln Asn

50 55 60

35 Leu Thr Gln Leu Lys Ala Ala Val Gly Glu Leu Ser Glu Lys Ser Lys
65 70 75 80

Leu Gln Glu Ile Tyr Gln Glu Leu Thr Gln Leu Lys Ala Ala Val Gly

85 90 95

87

	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	G1n	Glu	Ile	Tyr	Gln	Glu	Leu	Thr
				100					105					110		
	Arg	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	G1u	Lys	Ser	Lys	Leu	Gln
			115					120					125			
5	Glu	Ilė	Tyr	Gln	Glu	Leu	Thr	Arg	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu
		130					135					140				
	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	G1n	Glu	Leu	Thr	Arg	Leu
	145					150					155					160
	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile
10					165					170					175	
	Tyr	Gln	Glu	Leu	Thr	Glu	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	G1u
				180					185					190	•	
	Lys	Ser	Lys	Leu	Gln	G1u	Ile	Tyr	Gln	Glu	Leu	Thr	Gln	Leu	Lys	Ala
			195					200					205			
15	Ala	Val	Gly	Glu	Leu	Pro	Asp	Gln	Ser	Lys	Gln	Gln	Gln	Ile	Tyr	G1n
		210					215					220				
	Glu	Leu	Thr	Asp	Leu	Lys	Thr	Ala	Phe	Glu	Arg	Leu	Cys	Arg	His	Cys
	225					230				•	235					240
	Pro	Lys	Asp	Trp	Thr	Phe	Phe	Gln	Gly	Asn	Cys	Tyr	Phe	Met	Ser	Asn
20					245					250					255	
	Ser	Gln	Arg	Asn	Trp	His	Asp	Ser	Val	Thr	Ala	Cys	Gln	Glu	Val	Arg
				260					265					270		
	Ala	Gln	Leu	Val	Val	Ile	Lys	Thr	Ala	Glu	Glu	Gln	Leu	Pro	Ala	Val
			275					280					285			
25	Leu	Glu	Gln	Trp	Arg	Thr	G1n	Gln								
		290					295									

(2) INFORMATION FOR SEQ ID NO: 4:

30 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 197

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

35 (iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

88

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

5

Met Cys Thr Gly Lys Cys Ala Arg Cys Val Gly Leu Ser Leu Ile Thr

1 5 10 15

Leu Cys Leu Val Cys Ile Val Ala Asn Ala Leu Leu Leu Val Pro Asn
20 25 30

10 Gly Glu Thr Ser Trp Thr Asn Thr Asn His Leu Ser Leu Gln Val Trp

35 40 45

Leu Met Gly Gly Phe Ile Gly Gly Gly Leu Met Val Leu Cys Pro Gly 50 55 60

Ile Ala Ala Val Arg Ala Gly Gly Lys Gly Cys Cys Gly Ala Gly Cys

15 65 70 75 80

Cys Gly Asn Arg Cys Arg Met Leu Arg Ser Val Phe Ser Ser Ala Phe
85 90 95

Gly Val Leu Gly Ala Ile Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu 100 105 110

20 Arg Asn Gly Pro Arg Cys Leu Met Asn Gly Glu Trp Gly Tyr His Phe 115 120 125

Glu Asp Thr Ala Gly Ala Tyr Leu Leu Asn Arg Thr Leu Trp Asp Arg 130 135 140

Cys Glu Ala Pro Pro Arg Val Val Pro Trp Asn Val Thr Leu Phe Ser

25 145 150 155 160

Leu Leu Val Ala Ala Ser Cys Leu Glu Ile Val Leu Cys Gly Ile Gln
165 170 175

Leu Val Asn Ala Thr Ile Gly Val Phe Cys Gly Asp Cys Arg Lys Lys
180 185 190

30 Gln Asp Thr Pro His

195

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:

35 (A) LENGTH: 221

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

89

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 5 (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP01526

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

10	Met	Glu	Ala	Gly	Gly	Phe	Leu	Asp	Ser	Leu	Ile	Tyr	Gly	Ala	Cys	Va]
	1				5					10					15	
	Val	Phe	Thr	Leu	Gly	Met	Phe	Ser	Ala	Gly	Leu	Ser	Asp	Leu	Arg	Ris
				20					25					30		
	Met	Arg	Met	Thr	Arg	Ser	Val	Asp	Asn	Va1	G1n	Phe	Leu	Pro	Phe	Lei
15			35					40					45			
	Thr	Thr	Glu	Val	Asn	Asn	Leu	Gly	Trp	Leu	Ser	Tyr	Gly	Ala	Leu	Ly
		50					55					60				
	Gly	Asp	Gly	Ile	Leu	Ile	Val	Val	Asn	Thr	Val	Gly	Ala	Ala	Leu	Glı
	65					70					75					80
20	Thr	Leu	Tyr	Ile	Leu	Ala	Tyr	Leu	His	Tyr	Cys	Pro	Arg	Lys	Arg	Va]
					85					90					95	
	Val	Leu	Leu	Gln	Thr	Ala	Thr	Leu	Leu	Gly	Val	Leu	Leu	Leu	Gly	Ty
				100					105					110		
	Gly	Tyr	Phe	Trp	Leu	Leu	Val	Pro	Asn	Pro	G1u	Ala	Arg	Leu	Gln	Gli
25			115					120					125			
	Leu		Leu	Phe	Cys	Ser	Val	Phe	Thr	Ile	Ser	Met	Tyr	Leu	Ser	Pro
		130					135					140				
		Ala	Asp	Leu	Ala	Lys	Val	Ile	G1n	Thr	Lys	Ser	Thr	G1n	Cys	Le
	145					150					155					160
30	Ser	Tyr	Pro	Leu	Thr	Ile	Ala	Thr	Leu	Leu	Thr	Ser	Ala	Ser		Cy
					165					170					175	
	Leu	Tyr	Gly		Arg	Leu	Arg	Asp	Pro	Tyr	Ile	Met	Val	Ser	Asn	Pho
				180					185					190		
	Pro	Gly		Val	Thr	Ser	Phe		Arg	Phe	Trp	Leu	Phe	Trp	Lys	Ty
35			195					200					205			
	Pro		Glu	Gln	Asp	Arg		Tyr	Trp	Leu	Leu	Gln	Thr			
		210					215					220				

6:

(1 G)
90
(2) INFORMATION FOR SEQ ID NO: 6:
(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 251
(B) TYPE: Amino acid
(D) TOPOLOGY: Linear
(ii) SEQUENCE KIND: Protein
(iii) HYPOTHETICAL: No
(vi) ORIGINAL SOURCE:
(A) ORGANISM: Homo sapiens
(B) CELL KIND: Stomach cancer
(D) CLONE NAME: HP10230
(xi) SEQUENCE DESCRIPTION: SEQ ID NO
Met Ser Asp Ile Gly Asp Trp Phe Arg Ser Il
1 5 10

5

. 10

15

Met Ser Asp Ile Gly Asp Trp Phe Arg Ser Ile Pro Ala Ile Thr Arg

1 5 10 15

Tyr Trp Phe Ala Ala Thr Val Ala Val Pro Leu Val Gly Lys Leu Gly

20 25 30

20 Leu Ile Ser Pro Ala Tyr Leu Phe Leu Trp Pro Glu Ala Phe Leu Tyr

35 40 45

Arg Phe Gln Ile Trp Arg Pro Ile Thr Ala Thr Phe Tyr Phe Pro Val

Arg Phe Gln Ile Trp Arg Pro Ile Thr Ala Thr Phe Tyr Phe Pro Val
50 55 60

Gly Pro Gly Thr Gly Phe Leu Tyr Leu Val Asn Leu Tyr Phe Leu Tyr

75
80

Gln Tyr Ser Thr Arg Leu Glu Thr Gly Ala Phe Asp Gly Arg Pro Ala 85 90 95

Asp Tyr Leu Phe Met Leu Leu Phe Asn Trp Ile Cys Ile Val Ile Thr
100 105 110

30 Gly Leu Ala Met Asp Met Gln Leu Leu Met Ile Pro Leu Ile Met Ser 115 120 125

Val Leu Tyr Val Trp Ala Gln Leu Asn Arg Asp Met Ile Val Ser Phe 130 135 140

Trp Phe Gly Thr Arg Phe Lys Ala Cys Tyr Leu Pro Trp Val Ile Leu 35 145 150 155 160

Gly Phe Asn Tyr Ile Ile Gly Gly Ser Val Ile Asn Glu Leu Ile Gly

165 170 175

Asn Leu Val Gly His Leu Tyr Phe Phe Leu Met Phe Arg Tyr Pro Met

91

185 190 Asp Leu Gly Gly Arg Asn Phe Leu Ser Thr Pro Gln Phe Leu Tyr Arg 200 Trp Leu Pro Ser Arg Arg Gly Gly Val Ser Gly Phe Gly Val Pro Pro 5 215 Ala Ser Met Arg Arg Ala Ala Asp Gln Asn Gly Gly Gly Arg His 225 230 235 240 Asn Trp Gly Gln Gly Phe Arg Leu Gly Asp Gln 245 250 . 10 (2) INFORMATION FOR SEQ ID NO: 7: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 106 15 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 20 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Epidermoid carcinoma (C) CELL LINE: KB (D) CLONE NAME: HP10389 25 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7: Met Ala Thr Pro Gly Pro Val Ile Pro Glu Val Pro Phe Glu Pro Ser 10 Lys Pro Pro Val Ile Glu Gly Leu Ser Pro Thr Val Tyr Arg Asn Pro 20 25 Glu Ser Phe Lys Glu Lys Phe Val Arg Lys Thr Arg Glu Asn Pro Val Val Pro Ile Gly Cys Leu Ala Thr Ala Ala Ala Leu Thr Tyr Gly Leu 35 50 55 60 Tyr Ser Phe His Arg Gly Asn Ser Gln Arg Ser Gln Leu Met Met Arg

70

Thr Arg Ile Ala Ala Gln Gly Phe Thr Val Ala Ala Ile Leu Leu Gly

92

85 90 95

Leu Ala Val Thr Ala Met Lys Ser Arg Pro

100 105

5

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 78

· 10 (B) TYPE: Amino acid

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: Protein

(iii) HYPOTHETICAL: No

15 (vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10408

20 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Gly Ser Gly Leu Pro Leu Val Leu Leu Leu Thr Leu Leu Gly Ser

1 5 10 1

Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu Lys Leu Lys Glu

25 20 25 30

Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe Leu Glu Leu Leu

35 40 45

Glu Lys Leu Cys Leu Leu His Leu Pro Ser Gly Thr Ser Val Thr

50 55 60

30 Leu His His Ala Arg Ser Gln His His Val Val Cys Asn Thr

65 70 75

(2) INFORMATION FOR SEQ ID NO: 9:

35 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 314

(B) TYPE: Amino acid

(D) TOPOLOGY: Linear

93

(iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

5 (A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10412

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 9:

10

Met Val Ala Pro Val Trp Tyr Leu Val Ala Ala Ala Leu Leu Val Gly

1 5 10 15

Phe Ile Leu Phe Leu Thr Arg Ser Arg Gly Arg Ala Ala Ser Ala Gly

20 25 30

15 Gln Glu Pro Leu His Asn Glu Glu Leu Ala Gly Ala Gly Arg Val Ala

35 40 45
Gln Pro Gly Pro Leu Glu Pro Glu Glu Pro Arg Ala Gly Gly Arg Pro

50 55 60

Arg Arg Arg Arg Asp Leu Gly Ser Arg Leu Gln Ala Gln Arg Arg Ala

20 65 70 75 80

Gln Arg Val Ala Trp Ala Glu Ala Asp Glu Asn Glu Glu Glu Ala Val 85 90 95

Ile Leu Ala Gln Glu Glu Glu Gly Val Glu Lys Pro Ala Glu Thr His
100 105 110

25 Leu Ser Gly Lys Ile Gly Ala Lys Lys Leu Arg Lys Leu Glu Glu Lys

115 120 125
Gln Ala Arg Lys Ala Gln Arg Glu Ala Glu Glu Ala Glu Arg Glu Glu

130 135 140

Arg Lys Arg Leu Glu Ser Gln Arg Glu Ala Glu Trp Lys Lys Glu Glu

30 145 150 155 160

Glu Arg Leu Arg Leu Glu Glu Glu Glu Glu Glu Glu Glu Arg Lys
165 170 175

Ala Arg Glu Glu Gln Ala Gln Arg Glu His Glu Glu Tyr Leu Lys Leu 180 185 190

35 Lys Glu Ala Phe Val Val Glu Glu Glu Gly Val Gly Glu Thr Met Thr
195 200 205

Glu Glu Gln Ser Gln Ser Phe Leu Thr Glu Phe Ile Asn Tyr Ile Lys
210 215 220

94

Gln Ser Lys Val Val Leu Leu Glu Asp Leu Ala Ser Gln Val Gly Leu 235 Arg Thr Gln Asp Thr Ile Asn Arg Ile Gln Asp Leu Leu Ala Glu Gly 245 250 255 Thr Ile Thr Gly Val Ile Asp Asp Arg Gly Lys Phe Ile Tyr Ile Thr 265 Pro Glu Glu Leu Ala Ala Val Ala Asn Phe Ile Arg Gln Arg Gly Arg 275 280 285 Val Ser Ile Ala Glu Leu Ala Gln Ala Ser Asn Ser Leu Ile Ala Trp 10 295 300 Gly Arg Glu Ser Pro Ala Gln Ala Pro Ala 305 310

- 15 (2) INFORMATION FOR SEQ ID NO: 10:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 195
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
- 20 (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 25 (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10413
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 10:
- - Asp Gln Pro Ala Ala Ser Gly Asp Ser Asp Asp Glu Pro Pro Pro 50 55 60

 Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro Ala Glu Leu Arg Arg

95

70 65 75 Phe Asp Gly Val Gln Asp Pro Arg Ile Leu Met Ala Ile Asn Gly Lys 85 90 95 Val Phe Asp Val Thr Lys Gly Arg Lys Phe Tyr Gly Pro Glu Gly Pro 5 105 Tyr Gly Val Phe Ala Gly Arg Asp Ala Ser Arg Gly Leu Ala Thr Phe 115 120 Cys Leu Asp Lys Glu Ala Leu Lys Asp Glu Tyr Asp Asp Leu Ser Asp 135 10 Leu Thr Ala Ala Gln Gln Glu Thr Leu Ser Asp Trp Glu Ser Gln Phe 145 150 155 160 Thr Phe Lys Tyr His His Val Gly Lys Leu Leu Lys Glu Gly Glu Glu 165 170 Pro Thr Val Tyr Ser Asp Glu Glu Glu Pro Lys Asp Glu Ser Ala Arg 180 15 185 190 Lys Asn Asp 195 20 (2) INFORMATION FOR SEQ ID NO: 11:

- - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 462
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
- 25 (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 30 (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10415
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 11:
- 35 Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu Ala Leu Val 1 10 Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala Ala Gly Ile 20 25

	Pro	Gly	Ile	Thr	Pro	Thr	Glu	Glu	Lys	Asp	Gly	Asn	Leu	Pro	Asp	Ile
			35					40					45			
	Val	Asn	Ser	Gly	Ser	Leu	His	G1u	Phe	Leu	Val	Asn	Leu	His	Glu	Arg
		50					55					60				
5	Tyr	Gly	Pro	Val	Val	Ser	Phe	Trp	Phe	Gly	Arg	Arg	Leu	Val	Val	Ser
	65					70					75					80
	Leu	Gly	Thr	Val	Asp	Val	Leu	Lys	Gln	His	Ile	Asn	Pro	Asn	Lys	Thr
					85					90					95	
	Leu	Asp	Pro	Phe	Glu	Thr	Met	Leu	Lys	Ser	Leu	Leu	Arg	Tyr	Gln	Ser
10				100					105					110		
	Gly	Gly	Gly	Ser	Val	Ser	Glu	Asn	His	Met	Arg	Lys	Lys	Leu	Tyr	Glu
			115					120					125			
	Asn	Gly	Val	Thr	Asp	Ser	Leu	Lys	Ser	Asn	Phe	Ala	Leu	Leu	Leu	Lys
		130					135					140				
15	Leu	Ser	Glu	Glu	Leu	Leu	Asp	Lys	Trp	Leu	Ser	Tyr	Pro	Glu	Thr	Gln
	145					150					155					160
	His	Val	Pro	Leu	Ser	Gln	His	Met	Leu	Gly	Phe	Ala	Met	Lys	Ser	Val
					165					170					175	
	Thr	Gln	Met	Val	Met	Gly	Ser	Thr	Phe	Glu	Asp	Asp	Gln	Glu	Val	Ile
20				180					185					190		
	Arg	Phe	Gln	Lys	Asn	His	Gly	Thr	Val	Trp	Ser	Glu	Ile	Gly	Lys	Gly
			195					200					205			
	Phe	Leu	Asp	Gly	Ser	Leu	Asp	Lys	Asn	Met	Thr	Arg	Lys	Lys	Gln	Tyr
		210					215					220				
25	Glu	Asp	Ala	Leu	Met	Gln	Leu	Glu	Ser	Val	Leu	Arg	Asn	Ile	Ile	Lys
	225					230					235					240
	Glu	Arg	Lys	Gly	Arg	Asn	Phe	Ser	Gln	His	Ile	Phe	Ile	Asp	Ser	Leu
					245					250					255	
	Val	Gln	Gly	Asn	Leu	Asn	Asp	Gln	Gln	Ile	Leu	Glu	Asp	Ser	Met	Ile
30				260					265					270		
	Phe	Ser	Leu	Ala	Ser	Cys	Ile	Ile	Thr	Ala	Lys	Leu	Cys	Thr	Trp	Ala
			275					280					285			
	Ile	Cys	Phe	Leu	Thr	Thr	Ser	Glu	Glu	Val	Gln	Lys	Lys	Leu	Tyr	Glu
		290					295					300				
35	Glu	Ile	Asn	Gln	Val	Phe	Gly	Asn	Gly	Pro	Val	Thr	Pro	Glu	Lys	Ile
	305					310					315					320
	Glu	G1n	Leu	Arg	Tyr	Cys	Gln	His	Val	Leu	Cys	Glu	Thr	Val	Arg	Thr
					325					330					335	

97

Ala Lys Leu Thr Pro Val Ser Ala Gln Leu Gln Asp Ile Glu Gly Lys 345 Ile Asp Arg Phe Ile Ile Pro Arg Glu Thr Leu Val Leu Tyr Ala Leu 355 360 365 5 Gly Val Val Leu Gln Asp Pro Asn Thr Trp Pro Ser Pro His Lys Phe 375 380 Asp Pro Asp Arg Phe Asp Asp Glu Leu Val Met Lys Thr Phe Ser Ser 390 395 Leu Gly Phe Ser Gly Thr Gln Glu Cys Pro Glu Leu Arg Phe Ala Tyr 10 405 410 Met Val Thr Thr Val Leu Leu Ser Val Leu Val Lys Arg Leu His Leu 420 425 430 Leu Ser Val Glu Gly Gln Val Ile Glu Thr Lys Tyr Glu Leu Val Thr 440 15 Ser Ser Arg Glu Glu Ala Trp Ile Thr Val Ser Lys Arg Tyr 450 455 460

(2) INFORMATION FOR SEQ ID NO: 12:

20 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 247
- (B) TYPE: Amino acid
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: Protein
- 25 (iii) HYPOTHETICAL: No

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- 30 (D) CLONE NAME: HP10419

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 12:

Met Gly Ala Ala Val Phe Phe Gly Cys Thr Phe Val Ala Phe Gly Pro

35 1 5 5 1 10 15 15

Ala Phe Ala Leu Phe Leu Ile Thr Val Ala Gly Asp Pro Leu Arg Val

20 25 25 5 30

Ile Ile Leu Val Ala Gly Ala Phe Phe Trp Leu Val Ser Leu Leu Leu

		35					40					45			
Ala	Ser	Val	Val	Trp	Phe	Ile	Leu	Val	His	Val	Thr	Asp	Arg	Ser	Asp
	50					55					60				
Ala	Arg	Leu	Gln	Tyr	Gly	Leu	Leu	Ile	Phe	Gly	Ala	Ala	Val	Ser	Val
65					70					75					80
Leu	Leu	Gln	Glu	Val	Phe	Arg	Phe	Ala	Tyr	Tyr	Lys	Leu	Leu	Lys	Lys
				85					90					95	
Ala	Asp	Glu	Gly	Leu	Ala	Ser	Leu	Ser	Glu	Asp	Gly	Arg	Ser	Pro	Ile
			100					105					110		
Ser	Ile	Arg	Gln	Met	Ala	Tyr	Val	Ser	Gly	Leu	Ser	Phe	Gly	Ile	Ile
		115					120					125			
Ser	Gly	Val	Phe	Ser	Val	Ile	Asn	Ile	Leu	Ala	Asp	Ala	Leu	Gly	Pro
	130					135					140				
Gly	Val	Val	Gly	Ile	His	Gly	Asp	Ser	Pro	Tyr	Tyr	Phe	Leu	Thr	Ser
145					150					155	•				160
Ala	Phe	Leu	Thr	Ala	Ala	Ile	Ile	Leu	Leu	His	Thr	Phe	Trp	Gly	Val
				165					170					175	
Val	Phe	Phe	Asp	Ala	Cys	Glu	Arg	Arg	Arg	Tyr	Trp	Ala	Leu	Gly	Leu
			180					185					190		
Val	Val	Gly	Ser	His	Leu	Leu	Thr	Ser	Gly	Leu	Thr	Phe	Leu	Asn	Pro
		195					200					205			
Trp		Glu	Ala	Ser	Leu	Leu	Pro	Ile	Tyr	Ala	Val	Thr	Va1	Ser	Met
	210					215					220				
Gly	Leu	Trp	Ala	Phe	Ile	Thr	Ala	Gly	Gly	Ser	Leu	Arg	Ser	Ile	Gln
225					230					235					240
Arg	Ser	Leu	Leu	Cys	Lys	Asp									
				245											
	Ala 65 Leu Ala Ser Gly 145 Ala Val Trp Gly 225	50 Ala Arg 65 Leu Leu Ala Asp Ser Ile Ser Gly 130 Gly Val 145 Ala Phe Val Phe Val Val Trp Tyr 210 Gly Leu 225	Ala Ser Val 50 Ala Arg Leu 65 Leu Leu Gln Ala Asp Glu Ser Ile Arg 115 Ser Gly Val 130 Gly Val Val 145 Ala Phe Leu Val Phe Phe Val Val Gly Val Gly Trp Tyr Glu 210 Gly Leu Trp 225	Ala Ser Val Val 50 Ala Arg Leu Gln 65 Leu Leu Gln Glu Ala Asp Glu Gly 100 Ser Ile Arg Gln 115 Ser Gly Val Phe 130 Gly Val Val Gly 145 Ala Phe Leu Thr Val Phe Phe Asp 180 Val Val Gly Ser 195 Trp Tyr Glu Ala 210 Gly Leu Trp Ala 225	Ala Ser Val Val Trp 50 Ala Arg Leu Gln Tyr 65 Leu Leu Gln Glu Val 85 Ala Asp Glu Gly Leu 100 Ser Ile Arg Gln Mer 115 Ser Gly Val Phe Ser 130 Gly Val Val Gly Ile 145 Ala Phe Leu Thr Ala 165 Val Phe Asp Ala 180 Val Val Gly Ser His 195 Trp Tyr Glu Ala Ser 210 Gly Leu Trp Ala Phe 225 Arg Ser Leu Leu Cys	Ala Ser Val Val Trp Phe 50 50 70 61 70 70 65 70 61 70 70 Leu Leu 61 70 70 Ala Asp 61 61 70 70 Ala Asp 61 70 70 70 Ala Asp 61 70 <	Ala Ser Val Val Trp Phe Ile 50 Jew Gln Typ Gly Lew Ala Arg Lew Gln Typ Typ Lew Lew Gln Glw Val Phe Arg Ala Asp Glw Glw Ala Typ Ala Asp Glw Met Ala Typ Ala Yal Yal Phe Ser Val Ile Ala Phe Lew Thr Ala Ala Ile Ala Phe Lew Ala Ala Ile Ile Val Phe Asp Ala Cys Glw Val Val Glw Ser His Lew Lew Val Val Glw Ala Ser Lew Lew Trp Tyr Glw Ala Ser Lew Lew Lew Lew Ala Phe Ile Tyr Tr	Ala Ser Val Val Trp Phe Ile Leu 50	Ala Ser Val Val Trp Phe Ile Leu Val Ala Arg Leu Gln Tyr Gly Leu Leu Ile 65	Ala Ser Val Val Trp Phe Ile Leu Val His Ala Arg Leu Gln Tyr Gly Leu Leu Ile Phe 65	Ala Ser Val Val Trp Phe Ile Leu Val His Val Ala Arg Leu Gln Tyr Gly Leu Leu Ile Phe Gly Gly Gly Gly Free Gly Free Free Free Gly Free Free Gly Free Free Gly Free Free<	Ala Ser Val Val Trp Phe Ile Leu Val His Val Thr 60 Ala Arg Leu Gln Tyr Gly Leu Leu Ile Phe Gly Ala Ale Phe Ala Tyr Tyr Lyr Ala Tyr Tyr Lyr Ala Tyr Tyr Lyr Tyr Lyr Ly	Ala Ser Val Val Trp Phe IIe Leu Val His Val Thr Asp 50	Ala Ser Val Val Trp Phe Ile Leu Val His Val Thr Asp Arg 50	Ala Ser Val Val Trp Phe Ile Leu Val His Val Thr Asp Arg Ser 50

- 30 (2) INFORMATION FOR SEQ ID NO: 13:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 113
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
- 35 (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:

80

99

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- (D) CLONE NAME: HP10424
- 5 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 13:

Met Asn Phe Tyr Leu Leu Leu Ala Ser Ser Ile Leu Cys Ala Leu Ile

1 5 10 15

Val Phe Trp Lys Tyr Arg Arg Phe Gln Arg Asn Thr Gly Glu Met Ser

10 20 25 30

Ser Asn Ser Thr Ala Leu Ala Leu Val Arg Pro Ser Ser Gly Leu

Ile Asn Ser Asn Thr Asp Asn Asn Leu Ala Val Tyr Asp Leu Ser Arg

50 55 60 15 Asp Ile Leu Asn Asn Phe Pro His Ser Ile Ala Arg Gln Lys Arg Ile

Leu Val Asn Leu Ser Met Val Glu Asn Lys Leu Val Glu Leu Glu His
85 90 95

Thr Leu Leu Ser Lys Gly Phe Arg Gly Ala Ser Pro His Arg Lys Ser

20 100 105 110

70

Thr

- (2) INFORMATION FOR SEQ ID NO: 14:
- 25 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 365
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
- 30 (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Epidermoid carcinoma
- 35 (C) CELL LINE: KB
 - (D) CLONE NAME: HP10428
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 14:

	Met	Gly	Arg	Trp	Ala	Leu	Asp	Val	Ala	Phe	Leu	Trp	Lys	Ala	Val	Leu
	1				5					10					15	
	Thr	Leu	Gly	Leu	Val	Leu	Leu	Tyr	Tyr	Cys	Phe	Ser	Ile	Gly	Ile	Thr
				20					25					30		
5	Phe	Tyr	Asn	Lys	Trp	Leu	Thr	Lys	Ser	Phe	His	Phe	Pro	Leu	Phe	Met
			35					40					45			
	Thr	Met	Leu	His	Leu	Ala	Va1	Ile	Phe	Leu	Phe	Ser	Ala	Leu	Ser	Arg
		50					55					60				
•	Ala	Leu	Val	Gln	Сув	Ser	Ser	His	Arg	Ala	Arg	Val	Val	Leu	Ser	Trp
10	65					70					75					80
	Ala	Asp	Tyr	Leu	Arg	Arg	Val	Ala	Pro	Thr	Ala	Leu	Ala	Thr	Ala	Leu
					85					90					95	
	Asp	Val	G1y	Leu	Ser	Asn	Trp	Ser	Phe	Leu	Tyr	Val	Thr	Val	Ser	Leu
				100					105					110		
15	Tyr	Thr	Met	Thr	Lys	Ser	Ser	Ala	Val	Leu	Phe	Ile	Leu	Ile	Phe	Ser
			115					120					125			
	Leu	Ile	Phe	Lys	Leu	Glu	Glu	Leu	Arg	Ala	Ala	Leu	Va1	Leu	Val	Val
		130					135					140				
	Leu	Leu	Ile	Ala	Gly	Gly	Leu	Phe	Met	Phe	Thr	Tyr	Lys	Ser	Thr	Gln
20	145					150					155					160
	Phe	Asn	Val	Glu	Gly	Phe	Ala	Leu	Val	Leu	Gly	Ala	Ser	Phe	Ile	Gly
					165					170					175	
	Gly	Ile	Arg	Trp	Thr	Leu	Thr	Gln	Met	Leu	Leu	Gln	Lys	Ala	Glu	Leu
				180					185					190		
25	Gly	Leu	Gln	Asn	Pro	Ile	Asp	Thr	Met	Phe	His	Leu	Gln	Pro	Leu	Met
			195					200					205			
	Phe	Leu	Gly	Leu	Phe	Pro	Leu	Phe	Ala	Val	Phe	Glu	Gly	Leu	His	Leu
		210					215					220				
		Thr	Ser	Glu	Lys	Ile	Phe	Arg	Phe	Gln	Asp	Thr	Gly	Leu	Leu	Leu
30	225					230					235					240
	Arg	Val	Leu	Gly	Ser	Ļeu	Phe	Leu	Gly	Gly	Ile	Leu	Ala	Phe	Gly	Leu
					245					250					255	
	Gly	Phe	Ser	Glu	Phe	Leu	Leu	Val	Ser	Arg	Thr	Ser	Ser	Leu	Thr	Leu
				260					265					270		
35	Ser	Ile	Ala	Gly	Ile	Phe	Lys	Glu	Val	Cys	Thr	Leu	Leu	Leu	Ala	Ala
			275					280					285			
	His	Leu	Leu	Gly	Asp	Gln	Ile	Ser	Leu	Leu	Asn	Trp	Leu	Gly	Phe	Ala
		290					295					300				

101

 Leu Cys
 Leu Ser Gly
 Ile Ser Leu His Val Ala Leu Lys Ala Leu His

 305
 310
 315
 320

 Ser Arg Gly
 Asp Gly
 Gly Pro Lys Ala Leu Lys Gly Leu Gly Ser Ser
 325
 330
 335

 5 Pro Asp Leu Glu Leu Leu Leu Leu Arg Ser Ser Gln Arg Glu Glu Gly Asp
 340
 345
 350

 Asn Glu Glu Glu Glu Tyr Phe Val Ala Gln Gly Gln Gln
 365
 365

10

- (2) INFORMATION FOR SEQ ID NO: 15:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 226
 - (B) TYPE: Amino acid
- 15 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
- 20 (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10429
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 15:

25

Leu Val Leu Ser Leu Ile Thr Ser Leu Leu Ser Ser Gly Phe Thr Phe

102

100 105 110 Tyr Asn Ser Ile Ser Asn Pro Tyr Gln Thr Phe Leu Gly Pro Thr Gly 120 Val Tyr Thr Trp Asn Gly Leu Gly Ala Ser Phe Val Phe Val Thr Met 5 135 140 Ile Leu Phe Val Ala Asn Thr Gln Ser Asn Gln Leu Ser Glu Glu Leu 150 155 Phe Gln Met Leu Tyr Pro Ala Thr Thr Ser Lys Gly Thr Thr His Ser 170 10 Tyr Gly Tyr Ser Phe Trp Leu Ile Leu Leu Val Ile Leu Leu Asn Ile 185 Val Thr Val Thr Ile Ile Ile Phe Tyr Gln Lys Ala Arg Tyr Gln Arg 200 Lys Gln Glu Gln Arg Lys Pro Met Glu Tyr Ala Pro Arg Asp Gly Ile 15 215 220 Leu Phe 225

- 20 (2) INFORMATION FOR SEQ ID NO: 16:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 129
 - (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
- 25 (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 30 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP10432
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 16:
- 35 Met Ala Arg Gly Ser Leu Arg Arg Leu Leu Arg Leu Leu Val Leu Gly

 1 5 10 15

 Leu Trp Leu Ala Leu Leu Arg Ser Val Ala Gly Glu Gln Ala Pro Gly
 20 25 30

103

Thr Ala Pro Cys Ser Arg Gly Ser Ser Trp Ser Ala Asp Leu Asp Lys 40 Cys Met Asp Cys Ala Ser Cys Arg Ala Arg Pro His Ser Asp Phe Cys 50 55 5 Leu Gly Cys Ala Ala Ala Pro Pro Ala Pro Phe Arg Leu Leu Trp Pro 70 75 Ile Leu Gly Gly Ala Leu Ser Leu Thr Phe Val Leu Gly Leu Leu Ser 85 90 Gly Phe Leu Val Trp Arg Arg Cys Arg Arg Arg Glu Lys Phe Thr Thr 10 105 Pro Ile Glu Glu Thr Gly Gly Glu Gly Cys Pro Ala Val Ala Leu Ile 115 120 125 Gln

15

- (2) INFORMATION FOR SEQ ID NO: 17:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 163
- 20 (B) TYPE: Amino acid
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: Protein
 - (iii) HYPOTHETICAL: No
- 25 (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Liver
 - (D) CLONE NAME: HP10433
- 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 17:

104

60 50 55 Phe Val Arg Leu Glu Phe Lys Leu Gln Gln Thr Ser Cys Arg Lys Arg 65 Asp Trp Lys Lys Pro Glu Cys Lys Val Arg Pro Asn Gly Arg Lys Arg 5 90 Lys Cys Leu Ala Cys Ile Lys Leu Gly Ser Glu Asp Lys Val Leu Gly 100 105 110 Arg Leu Val His Cys Pro Ile Glu Thr Gln Val Leu Arg Glu Ala Glu 120 Glu His Gln Glu Thr Gln Cys Leu Arg Val Gln Arg Ala Gly Glu Asp 10 130 135 140 Pro His Ser Phe Tyr Phe Pro Gly Gln Phe Ala Phe Ser Lys Ala Leu 150 155 145 Pro Arg Ser 15 (2) INFORMATION FOR SEQ ID NO: 18: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 193 20 (B) TYPE: Amino acid (D) TOPOLOGY: Linear (ii) SEQUENCE KIND: Protein (iii) HYPOTHETICAL: No 25 (vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens (B) CELL KIND: Stomach cancer (D) CLONE NAME: HP10480 30 (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 18: Met Ile Arg Cys Gly Leu Ala Cys Glu Arg Cys Arg Trp Ile Leu Pro Leu Leu Leu Ser Ala Ile Ala Phe Asp Ile Ile Ala Leu Ala Gly 35 20 25 Arg Gly Trp Leu Gln Ser Ser Asp His Gly Gln Thr Ser Ser Leu Trp 40

Trp Lys Cys Ser Gln Glu Gly Gly Gly Ser Gly Ser Tyr Glu Glu Gly

		50					55					60						
	Cys	Gln	Ser	Leu	Met	Glu	Tyr	Ala	Trp	Gly	Arg	Ala	Ala	Ala	Ala	Met		
	65					70					75					80		
	Leu	Phe	Cys	Gly	Phe	Ile	Ile	Leu	Val	Ile	Cys	Phe	Ile	Leu	Ser	Phe		
5					85					90					95			
	Phe	Ala	Leu	Cys	Gly	Pro	Gln	Met	Leu	Val	Phe	Leu	Arg	Val	Ile	Gly		
				100					105					110				
	Gly	Leu	Leu	Ala	Leu	Ala	Ala	Val	Phe	Gln	Ile	Ile	Ser	Leu	Val	Ile		
		•	115					120					125					
10	Tyr	Pro	Val	Lys	Tyr	Thr	Gln	Thr	Phe	Thr	Leu	His	Ala	Asn	Arg	Ala		
		130					135					140						
	Val	Thr	Tyr	Ile	Tyr	Asn	Trp	Ala	Tyr	Gly	Phe	Gly	Trp	Ala	Ala	Thr		
	145					150					155					160		
	Ile	Ile	Leu	Ile	Gly	Cys	Ala	Phe	Phe	Phe	Cys	Cys	Leu	Pro	Asn	Tyr		
15					165					170					175			
	Glu	Asp	Asp	Leu	Leu	Gly	Asn	Ala	Lys	Pro	Arg	Tyr	Phe	Tyr	Thr	Ser		
	•			180					185					190				
	Ala																	
	•																	
20																		
	(2)					-		10: 1										
		(:	1) SI					RISTI	CS:									
					LENG													
25								ic ac										
23								5: Do		2								
		()	141 (inear										
		(.	L I) (sEQUI	SHCE	KINI); CI	ONA t	O mr	LNA								
		(3	,;) (ופדפו	INAL	COIT	CF.											
30		,,	,_, (omo s	ani.									
								inea.	_	:115								
								HP01										
				(2)	0201	111	иш.	111 01	.203									
		()	ci) S	SEOU	ENCE	DESC	ית דאי:	rion:	SEC	מזו	NO.	10.						
35		,-	,	_ , ~ .					524			1).						
	ATG	GTC	rgc 1	CCT	rccca	T GO	CACI	CTGC	: ልፐር	СТАС	TCC	ጥ ር ጥር	ርሞርብ	CG A	GCAA	TGTCT		50
																CCGAT		20
																GCTAT		30
																~~***	10	- 0

106

	GTGCTGAGAC	TCAACCGAGT	GAACGACGCC	CAGGAATACA	GACGGGGTGG	CCTGGGATCT	240
	CTGTTCTATC	TTACACTGGA	TGTGCTAGAG	ACTGACTGCC	ATGTGCTCAG	AAAGAAGGCA	300
	TGGCAAGACT	GTGGAATGAG	GATATTTTT	GAATCAGTTT	ATGGTCAATG	CAAAGCAATA	360
	TTTTATATGA	ACAACCCAAG	TAGAGTTCTC	TATTTAGCTG	CTTATAACTG	TACTCTTCGC	420
5	CCAGTTTCAA	AAAAAAAGAT	TTACATGACG	TGCCCTGACT	GCCCAAGCTC	CATACCCACT	480
	GACTCTTCCA	ATCACCAAGT	GCTGGAGGCT	GCCACCGAGT	CTCTTGCGAA	ATACAACAAT	540
	GAGAACACAT	CCAAGCAGTA	TTCTCTCTTC	AAAGTCACCA	GGGCTTCTAG	CCAGTGGGTG	600
	GTCGGCCCTT	CTTACTTTGT	GGAATACTTA	ATTAAAGAAT	CACCATGTAC	TAAATCCCAG	660
	GCCAGCAGCT	GTTCACTTCA	GTCCTCCGAC	TCTGTGCCTG	TTGGTCTTTG	CAAAGGTTCT	720
10	CTGACTCGAA	CACACTGGGA	AAAGTTTGTC	TCTGTGACTT	GTGACTTCTT	TGAATCACAG	780
	GCTCCAGCCA	CTGGAAGTGA	AAACTCTGCT	GTTAACCAGA	AACCTACAAA	CCTTCCCAAG	840
	GTGGAAGAAT	CCCAGCAGAA	AAACACCCCC	CCAACAGACT	CCCCTCCAA	AGCTGGGCCA	900
	AGAGGATCTG	TCCAATATCT	TCCTGACTTG	GATGATAAAA	ATTCCCAGGA	AAAGGGCCCT	960
	CAGGAGGCCT	TTCCTGTGCA	TCTGGACCTA	ACCACGAATC	CCCAGGGAGA	AACCCTGGAT	1020
15	ATTTCCTTCC	TCTTCCTGGA	GCCTATGGAG	GAGAAGCTGG	TTGTCCTGCC	TTTCCCCAAA	1080
	GAAAAAGCAC	GCACTGCTGA	GTGCCCAGGG	CCAGCCCAGA	ATGCCAGCCC	TCTTGTCCTT	1140
	CCGCCA						1146

20 (2) INFORMATION FOR SEQ ID NO: 20:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 951
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 25 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 30 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP01299
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 20:
- ATGTGGCTCT ACCTGGCGGC CTTCGTGGGC CTGTACTACC TTCTGCACTG GTACCGGGAG
 AGGCAGGTGG TGAGCCACCT CCAAGACAAG TATGTCTTTA TCACGGGCTG TGACTCGGGC
 120
 TTTGGGAACC TGCTGGCCAG ACAGCTGGAT GCACGAGGCT TGAGAGTGCT GGCTGCGTGT
 180
 CTGACGGAGA AGGGGGCCGA GCAGCTGAGG GGCCAGACGT CTGACAGGCT GGAGACGGTG
 240

	ACCCTGGATG	TTACCAAGAT	GGAGAGCATC	GCTGCAGCTA	CTCAGTGGGT	GAAGGAGCAT	300
	GTGGGGGACA	GAGGACTCTG	GGGACTGGTG	AACAATGCAG	GCATTCTTAC	ACCAATTACC	360
	TTATGTGAGT	GGCTGAACAC	TGAGGACTCT	ATGAATATGC	TCAAAGTGAA	CCTCATTGGT	420
	GTGATCCAGG	TGACCTTGAG	CATGCTTCCT	TTGGTGAGGA	GAGCACGGGG	AAGAATTGTC	480
5	AATGTCTCCA	GCATTCTGGG	AAGAGTTGCT	TTCTTTGTAG	GAGGCTACTG	TGTCTCCAAG	540
	TATGGAGTGG	AAGCCTTTTC	AGATATTCTG	AGGCGTGAGA	TTCAACATTT	TGGGGTGAAA	600
	ATCAGCATAG	TTGAACCTGG	CTACTTCAGA	ACGGGAATGA	CAAACATGAC	ACAGTCCTTA	660
	GAGCGAATGA	AGCAAAGTTG	GAAAGAAGCC	CCCAAGCATA	TTAAGGAGAC	CTATGGACAG	720
	CAGTATTTTG	ATGCCCTTTA	CAATATCATG	AAGGAAGGGC	TGTTGAATTG	TAGCACAAAC	780
10	CTGAACCTGG	TCACTGACTG	CATGGAACAT	GCTCTGACAT	CGGTGCATCC	GCGAACTCGA	840
	TATTCAGCTG	GCTGGGATGC	TAAATTTTTC	TTCATCCCTC	TATCTTATTT	ACCTACATCA	900
•	CTGGCAGACT	ACATTTTGAC	TAGATCTTGG	CCCAAACCAG	CCCAGGCAGT	C	951

15 (2) INFORMATION FOR SEQ ID NO: 21:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 888
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 20 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 25 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP01347

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 21:

30	ATGAGTGACT	CCAAGGAACC	AAGGGTGCAG	CAGCTGGGCC	TCCTGGGGTG	TCTTGGCCAT	60
	GGCGCCCTGG	TGCTGCAACT	CCTCTCCTTC	ATGCTCTTGG	CTGGGGTCCT	GGTGGCCATC	120
	CTTGTCCAAG	TGTCCAAGGT	CCCCAGCTCC	CTAAGTCAGG	AACAATCCGA	GCAAGACGCA	180
	ATCTACCAGA	ACCTGACCCA	GCTTAAAGCT	GCAGTGGGTG	AGCTCTCAGA	GAAATCCAAG	240
	CTGCAGGAGA	TCTACCAGGA	GCTGACCCAG	CTGAAGGCTG	CAGTGGGTGA	GTTGCCAGAG	300
35	AAATCCAAGC	TGCAGGAGAT	CTACCAGGAG	CTGACCCGGC	TGAAGGCTGC	AGTGGGTGAG	360
	TTGCCAGAGA	AATCCAAGCT	GCAGGAGATC	TACCAGGAGC	TGACCCGGCT	GAAGGCTGCA	420
	GTGGGTGAGT	TGCCAGAGAA	ATCCAAGCTG	CAGGAGATCT	ACCAGGAGCT	GACCCGGCTG	480
	AAGGCTGCAG	TGGGTGAGTT	GCCAGAGAAA	TCCAAGCTGC	AGGAGATCTA	CCAGGAGCTG	540

108

	ACGGAGCTGA	AGGCTGCAGT	GGGTGAGTTG	CCAGAGAAAT	CCAAGCTGCA	GGAGATCTAC	600
	CAGGAGCTGA	CCCAGCTGAA	GGCTGCAGTG	GGTGAGTTGC	CAGACCAGTC	CAAGCAGCAG	660
	CAAATCTATC	AAGAACTGAC	CGATTTGAAG	ACTGCATTTG	AACGCCTGTG	CCGCCACTGT	720
	CCCAAGGACT	GGACATTCTT	CCAAGGAAAC	TGTTACTTCA	TGTCTAACTC	CCAGCGGAAC	780
5	TGGCACGACT	CCGTCACCGC	CTGCCAGGAA	GTGAGGGCCC	AGCTCGTCGT	AATCAAAACT	840
	GCTGAGGAGC	AGCTTCCAGC	GGTACTGGAA	CAGTGGAGAA	CCCAACAA		888

(2) INFORMATION FOR SEQ ID NO: 22:

10 (i) SEQUENCE CHARACTERISTICS:

- (A) LENGTH: 591
- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- 15 (ii) SEQUENCE KIND: cDNA to mRNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Stomach cancer
- 20 (D) CLONE NAME: HP01440

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 22:

	ATGTGTACGG	GAAAATGTGC	CCGCTGTGTG	GGGCTCTCCC	TCATTACCCT	CTGCCTCGTC	60
25	TGCATTGTGG	CCAACGCCCT	CCTGCTGGTA	CCTAATGGGG	AGACCTCCTG	GACCAACACC	120
	AACCATCTCA	GCTTGCAAGT	CTGGCTCATG	GGCGGCTTCA	TTGGCGGGGG	CCTAATGGTA	180
	CTGTGTCCGG	GGATTGCAGC	CGTTCGGGCA	GGGGGCAAGG	GCTGCTGTGG	TGCTGGGTGC	240
	TGTGGAAACC	GCTGCAGGAT	GCTGCGCTCG	GTCTTCTCCT	CGGCGTTCGG	GGTGCTTGGT	300
	GCCATCTACT	GCCTCTCGGT	GTCTGGAGCT	GGGCTCCGAA	ATGGACCCAG	ATGCTTAATG	360
30	AACGGCGAGT	GGGGCTACCA	CTTCGAAGAC	ACCGCGGGAG	CTTACTTGCT	CAACCGCACT	420
	CTATGGGATC	GGTGCGAGGC	GCCCCTCGC	GTGGTCCCCT	GGAATGTGAC	GCTCTTCTCG	480
	CTGCTGGTGG	CCGCCTCCTG	CCTGGAGATA	GTACTGTGTG	GGATCCAGCT	GGTGAACGCG	540
	ACCATTGGTG	TCTTCTGCGG	CGATTGCAGG	AAAAAACAGG	ACACCCCTCA	С	591

- (2) INFORMATION FOR SEQ ID NO: 23:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 663

	109	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
5		
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP01526	
10		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 23:	
•		
	ATGGAGGCGG GCGGCTTTCT GGACTCGCTC ATTTACGGAG CATGCGTGGT CTTCACCCTT	60
	GGCATGTTCT CCGCCGGCCT CTCGGACCTC AGGCACATGC GAATGACCCG GAGTGTGGAC	120
15	AACGTCCAGT TCCTGCCCTT TCTCACCACG GAAGTCAACA ACCTGGGCTG GCTGAGTTAT	180
	GGGGCTTTGA AGGGAGACGG GATCCTCATC GTCGTCAACA CAGTGGGTGC TGCGCTTCAG	240
	ACCCTGTATA TCTTGGCATA TCTGCATTAC TGCCCTCGGA AGCGTGTTGT GCTCCTACAG	300
	ACTGCAACCC TGCTAGGGGT CCTTCTCCTG GGTTATGGCT ACTTTTGGCT CCTGGTACCC	360
	AACCCTGAGG CCCGGCTTCA GCAGTTGGGC CTCTTCTGCA GTGTCTTCAC CATCAGCATG	420
20	TACCTCTCAC CACTGGCTGA CTTGGCTAAG GTGATTCAAA CTAAATCAAC CCAATGTCTC	480
	TCCTACCCAC TCACCATTGC TACCCTTCTC ACCTCTGCCT CCTGGTGCCT CTATGGGTTT	540
	CGACTCAGAG ATCCCTATAT CATGGTGTCC AACTTTCCAG GAATCGTCAC CAGCTTTATC	600
	CGCTTCTGGC TTTTCTGGAA GTACCCCCAG GAGCAAGACA GGAACTACTG GCTCCTGCAA	660
	ACC	663
25		
	·	
	(2) INFORMATION FOR SEQ ID NO: 24:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 753	
30	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
25		
35	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10230

110

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 24:

	ATGTCGGACA	TCGGAGACTG	GTTCAGGAGC	ATCCCGGCGA	TCACGCGCTA	TTGGTTCGCC	60
	GCCACCGTCG	CCGTGCCCTT	GGTCGGCAAA	CTCGGCCTCA	TCAGCCCGGC	CTACCTCTTC	120
5	CTCTGGCCCG	AAGCCTTCCT	TTATCGCTTT	CAGATTTGGA	GGCCAATCAC	TGCCACCTTT	180
	TATTTCCCTG	TGGGTCCAGG	AACTGGATTT	CTTTATTTGG	TCAATTTATA	TTTCTTATAT	240
	CAGTATTCTA	CGCGACTTGA	AACAGGAGCT	TTTGATGGGA	GGCCAGCAGA	CTATTTATTC	300
	ATGCTCCTCT	TTAACTGGAT	TTGCATCGTG	ATTACTGGCT	TAGCAATGGA	TATGCAGTTG	360
	CTGATGATTC	CTCTGATCAT	GTCAGTACTT	TATGTCTGGG	CCCAGCTGAA	CAGAGACATG	420
10	ATTGTATCAT	TTTGGTTTGG	AACACGATTT	AAGGCCTGCT	ATTTACCCTG	GGTTATCCTT	480
	GGATTCAACT	ATATCATCGG	AGGCTCGGTA	ATCAATGAGC	TTATTGGAAA	TCTGGTTGGA	540
	CATCTTTATT	TTTTCCTAAT	GTTCAGATAC	CCAATGGACT	TGGGAGGAAG	AAATTTTCTA	600
	TCCACACCTC	AGTTTTTGTA	CCGCTGGCTG	CCCAGTAGGA	GAGGAGGAGT	ATCAGGATTT	660
	GGTGTGCCCC	CTGCTAGCAT	GAGGCGAGCT	GCTGATCAGA	ATGGCGGAGG	CGGGAGACAC	720
15	AACTGGGGCC	AGGGCTTTCG	ACTTGGAGAC	CAG			753

(2) INFORMATION FOR SEQ ID NO: 25:

(i) SEQUENCE CHARACTERISTICS:

20 (A) LENGTH: 318

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

25

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Epidermoid carcinoma

(C) CELL LINE: KB

30 (D) CLONE NAME: HP10389

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 25:

	ATGGCGACTC	CCGGCCCTGT	GATTCCGGAG	GTCCCCTTTG	AACCATCGAA	GCCTCCAGTC	60
35	ATTGAGGGGC	TGAGCCCCAC	TGTTTACAGG	AATCCAGAGA	GTTTCAAGGA	AAAGTTCGTT	120
	CGCAAGACCC	GCGAGAACCC	GGTGGTACCC	ATAGGTTGCC	TGGCCACGGC	GGCCGCCCTC	180
	ACCTACGGCC	TCTACTCCTT	CCACCGGGGC	AACAGCCAGC	GCTCTCAGCT	CATGATGCGC	240
	ACCCGGATCG	CCGCCCAGGG	TTTCACGGTC	GCAGCCATCT	TGCTGGGTCT	GGCTGTCACT	300

111

GCTATGAAGT CTCGACCC	318
---------------------	-----

	(2) INFORMATION FOR SEQ ID NO: 26:	
5	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 234	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
LO	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
15	(D) CLONE NAME: HP10408	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 26:	
	·	
	ATGGGGTCTG GGCTGCCCCT TGTCCTCCTC TTGACCCTCC TTGGCAGCTC ACATGGAACA	60
20	GGGCCGGGTA TGACTTTGCA ACTGAAGCTG AAGGAGTCTT TTCTGACAAA TTCCTCCTAT	120
	GAGTCCAGCT TCCTGGAATT GCTTGAAAAG CTCTGCCTCC TCCTCCATCT CCCTTCAGGG	180
	ACCAGCGTCA CCCTCCACCA TGCAAGATCT CAACACCATG TTGTCTGCAA CACA	234
25	(2) INFORMATION FOR SEQ ID NO: 27:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 942	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
30	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
35	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10412	

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 27:

	ATGGTGGCGC	CTGTGTGGTA	CTTGGTAGCG	GCGGCTCTGC	TAGTCGGCTT	TATCCTCTTC	60
	CTGACTCGCA	GCCGGGGCCG	GGCGGCATCA	GCCGGCCAAG	AGCCACTGCA	CAATGAGGAG	120
	CTGGCAGGAG	CAGGCCGGGT	GGCCCAGCCT	GGGCCCCTGG	AGCCTGAGGA	GCCGAGAGCT	180
	GGAGGCAGGC	CTCGGCGCCG	GAGGGACCTG	GGCAGCCGCC	TACAGGCCCA	GCGTCGAGCC	240
5	CAGCGGGTGG	CCTGGGCAGA	AGCAGATGAG	AACGAGGAGG	AAGCTGTCAT	CCTAGCCCAG	300
	GAGGAGGAAG	GTGTCGAGAA	GCCAGCGGAA	ACTCACCTGT	CGGGGAAAAT	TGGAGCTAAG	360
	AAACTGCGGA	AGCTGGAGGA	GAAACAAGCG	CGAAAGGCCC	AGCGTGAGGC	AGAGGAGGCT	420
	GAACGTGAGG	AGCGGAAACG	ACTCGAGTCC	CAGCGCGAAG	CTGAGTGGAA	GAAGGAGGAG	480
	GAGCGGCTTC	GCCTGGAGGA	GGAGCAGAAG	GAGGAGGAGG	AGAGGAAGGC	CCGCGAGGAG	540
10	CAGGCCCAGC	GGGAGCATGA	GGAGTACCTG	AAACTGAAGG	AGGCCTTTGT	GGTGGAGGAG	600
	GAAGGCGTAG	GAGAGACCAT	GACTGAGGAA	CAGTCCCAGA	GCTTCCTGAC	AGAGTTCATC	660
	AACTACATCA	AGCAGTCCAA	GGTTGTGCTC	TTGGAAGACC	TGGCTTCCCA	GGTGGGCCTA	720
	CGCACTCAGG	ACACCATAAA	TCGCATCCAG	GACCTGCTGG	CTGAGGGGAC	TATAACAGGT	780
	GTGATTGACG	ACCGGGGCAA	GTTCATCTAC	ATAACCCCAG	AGGAACTGGC	CGCCGTGGCC	840
15	AACTTCATCC	GACAGCGGGG	CCGGGTGTCC	ATCGCCGAGC	TTGCCCAAGC	CAGCAACTCC	900
	CTCATCGCCT	GGGGCCGGGA	GTCCCCTGCC	CAAGCCCCAG	CC		942

(2) INFORMATION FOR SEQ ID NO: 28:

20 (i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 585

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

25 (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

30 (D) CLONE NAME: HP10413

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 28:

	ATGGCTGCCG	AGGATGTGGT	GGCGACTGGC	GCCGACCCAA	GCGATCTGGA	GAGCGGCGGG	60
35	CTGCTGCATG	AGATTTTCAC	GTCGCCGCTC	AACCTGCTGC	TGCTTGGCCT	CTGCATCTTC	120
	CTGCTCTACA	AGATCGTGCG	CGGGGACCAG	CCGGCGGCCA	GCGGCGACAG	CGACGACGAC	180
	GAGCCGCCCC	CTCTGCCCCG	CCTCAAGCGG	CGCGACTTCA	CCCCGCCGA	GCTGCGGCGC	240
	TTCGACGGCG	TCCAGGACCC	GCGCATACTC	ATGCCCATCA	ACCCCAACCT	СТТССАТСТС	300

113

5	TCAGATGAGG	AAGAACCAAA	AGATGAGAGT	GCCCGGAAAA	ATGAT		585
	ACTTTCAAGT	ATCATCACGT	GGGCAAACTG	CTGAAGGAGG	GGGAGGAGCC	CACTGTGTAC	540
	GACCTTTCTG	ACCTCACTGC	TGCCCAGCAG	GAGACTCTGA	GTGACTGGGA	GTCTCAGTTC	480
	GCATCCAGGG	GCCTTGCCAC	ATTTTGCCTG	GATAAGGAAG	CACTGAAGGA	TGAGTACGAT	420
	ACCAAAGGCC	GCAAATTCTA	CGGGCCCGAG	GGGCCGTATG	GGGTCTTTGC	TGGAAGAGAT	360

(2) INFORMATION FOR SEQ ID NO: 29:

(i) SEQUENCE CHARACTERISTICS:

10

- (A) LENGTH: 1386
- (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double
- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: cDNA to mRNA

15

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- (D) CLONE NAME: HP10415

20

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 29:

	ATGTTGGACT	TCGCGATCTT	CGCCGTTACC	TTCTTGCTGG	CGTTGGTGGG	AGCCGTGCTC	. 60
	TACCTCTATC	CGGCTTCCAG	ACAAGCTGCA	GGAATTCCAG	GGATTACTCC	AACTGAAGAA	120
25	AAAGATGGTA	ATCTTCCAGA	TATTGTGAAT	AGTGGAAGTT	TGCATGAGTT	CCTGGTTAAT	180
	TTGCATGAGA	GATATGGGCC	TGTGGTCTCC	TTCTGGTTTG	GCAGGCGCCT	CGTGGTTAGT	240
	TTGGGCACTG	TTGATGTACT	GAAGCAGCAT	ATCAATCCCA	ATAAGACATT	GGACCCTTTT	300
	GAAACCATGC	TGAAGTCATT	ATTAAGGTAT	CAATCTGGTG	GTGGCAGTGT	GAGTGAAAAC	360
	CACATGAGGA	AAAAATTGTA	TGAAAATGGT	GTGACTGATT	CTCTGAAGAG	TAACTTTGCC-	420
30	CTCCTCCTAA	AGCTTTCAGA	AGAATTATTA	GATAAATGGC	TCTCCTACCC	AGAGACCCAG	480
	CACGTGCCCC	TCAGCCAGCA	TATGCTTGGT	TTTGCTATGA	AGTCTGTTAC	ACAGATGGTA	540
	ATGGGTAGTA	CATTTGAAGA	TGATCAGGAA	GTCATTCGCT	TCCAGAAGAA	TCATGGCACA	600
	GTTTGGTCTG	AGATTGGAAA	AGGCTTTCTA	GATGGGTCAC	TTGATAAAAA	CATGACTCGG	660
	AAAAAACAAT	ATGAAGATGC	CCTCATGCAA	CTGGAGTCTG	TTTTAAGGAA	CATCATAAAA	720
35	GAACGAAAAG	GAAGGAACTT	CAGTCAACAT	ATTTTCATTG	ACTCCTTAGT	ACAAGGGAAC	780
	CTTAATGACC	AACAGATCCT	AGAAGACAGT	ATGATATTTT	CTCTGGCCAG	TTGCATAATA	840
	ACTGCAAAAT	TGTGTACCTG	GGCAATCTGT	TTTTTAACCA	CCTCTGAAGA	AGTTCAAAAA	900
	AAATTATATG	AAGAGATAAA	CCAAGTTTTT	GGAAATGGTC	CTGTTACTCC	AGAGAAAATT	960

114

GAGCAGCTCA	GATATTGTCA	GCATGTGCTT	TGTGAAACTG	TTCGAACTGC	CAAACTGACT	1020
CCAGTTTCTG	CCCAGCTTCA	AGATATTGAA	GGAAAAATTG	ACCGATTTAT	TATTCCTAGA	1080
GAGACCCTCG	TCCTTTATGC	CCTTGGTGTG	GTACTTCAGG	ATCCTAATAC	TTGGCCATCT	1140
CCACACAAGT	TTGATCCAGA	TCGGTTTGAT	GATGAATTAG	TAATGAAAAC	TTTTTCCTCA	1200
CTTGGATTCT	CAGGCACACA	GGAGTGTCCA	GAGTTGAGGT	TTGCATATAT	GGTGACCACA	1260
GTACTTCTTA	GTGTATTGGT	GAAGAGACTG	CACCTACTTT	CTGTGGAGGG	ACAGGTTATT	1320
GAAACAAAGT	ATGAACTGGT	AACATCATCA	AGGGAAGAAG	CTTGGATCAC	TGTCTCAAAG	1380
AGATAT						1386

10

5

(2) INFORMATION FOR SEQ ID NO: 30:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 741
 - (B) TYPE: Nucleic acid
- 15 (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

20 (A) ORGANISM: Homo sapiens

(B) CELL KIND: Stomach cancer

(D) CLONE NAME: HP10419

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 30:

25

30

ATGGGGGCTG CG	GTGTTTTT	CGGCTGCACT	TTCGTCGCGT	TCGGCCCGGC	CTTCGCGCTT	60
TTCTTGATCA CT	GTGGCTGG	GGACCCGCTT	CGCGTTATCA	TCCTGGTCGC	AGGGGCATTT	120
TTCTGGCTGG TC	TCCCTGCT	CCTGGCCTCT	GTGGTCTGGT	TCATCTTGGT	CCATGTGACC	180
GACCGGTCAG AT	GCCCGGCT	CCAGTACGGC	CTCCTGATTT	TTGGTGCTGC	TGTCTCTGTC	240
CTTCTACAGG AG	GTGTTCCG	CTTTGCCTAC	TACAAGCTGC	TTAAGAAGGC	AGATGAGGGG	300
TTAGCATCGC TG	AGTGAGGA	CGGAAGATCA	CCCATCTCCA	TCCGCCAGAT	GGCCTATGTT	360
TCTGGTCTCT CC	TTCGGTAT	CATCAGTGGT	GTCTTCTCTG	TTATCAATAT	TTTGGCTGAT	420
GCACTTGGGC CA	.GGTGTGGT	TGGGATCCAT	GGAGACTCAC	CCTATTACTT	CCTGACTTCA	480
GCCTTTCTGA CA	GCAGCCAT	TATCCTGCTC	CATACCTTTT	GGGGAGTTGT	GTTCTTTGAT	540
GCCTGTGAGA GG	AGACGGTA	CTGGGCTTTG	GGCCTGGTGG	TTGGGAGTCA	CCTACTGACA	600
TCGGGACTGA CA	TTCCTGAA	CCCCTGGTAT	GAGGCCAGCC	TGCTGCCCAT	CTATGCAGTC	660
ACTGTTTCCA TG	GGGCTCTG	GGCCTTCATC	ACAGCTGGAG	GGTCCCTCCG	AAGTATTCAG	720
CGCAGCCTCT TG	TGTAAGGA	С				741

	(2) INFORMATION FOR SEQ ID NO: 31:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 339	
5	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
10	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10424	
_		
15	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 31:	
	A TICA A COTTOCOTA A DEPOSITA A COCA	
	ATGAACTTCT ATTTACTCCT AGCGAGCAGC ATTCTGTGTG CCTTGATTGT CTTCTGGAAA	60
	TATCGCCGCT TTCAGAGAAA CACTGGCGAA ATGTCATCAA ATTCAACTGC TCTTGCACTA	120
20	GTGAGACCCT CTTCTTCTGG GTTAATTAAC AGCAATACAG ACAACAATCT TGCAGTCTAC	180
20	GACCTCTCTC GGGATATTTT AAATAATTTC CCACACTCAA TAGCCAGGCA GAAGCGAATA	240
	TTGGTAAACC TCAGTATGGT GGAAAACAAG CTGGTTGAAC TGGAACATAC TCTACTTAGC AAGGGTTTCA GAGGTGCATC ACCTCACCGG AAATCCACC	300
	MIDDOTTION GRADIOCATO ROCTOROGGO HARTCOROG	339
25	(2) INFORMATION FOR SEQ ID NO: 32:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1095	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
30	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
35	(B) CELL KIND: Epidermoid carcinoma	
	(C) CELL LINE: KB	

(D) CLONE NAME: HP10428

116

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 32:

	ATGGGGAGGT	GGGCCCTCGA	TGTGGCCTTT	TTGTGGAAGG	CGGTGTTGAC	CCTGGGGCTG	60
	GTGCTTCTCT	ACTACTGCTT	CTCCATCGGC	ATCACCTTCT	ACAACAAGTG	GCTGACAAAG	120
5	AGCTTCCATT	TCCCCCTCTT	CATGACGATG	CTGCACCTGG	CCGTGATCTT	CCTCTTCTCC	180
	GCCCTGTCCA	GGGCGCTGGT	TCAGTGCTCC	AGCCACAGGG	CCCGTGTGGT	GCTGAGCTGG	240
	GCCGACTACC	TCAGAAGAGT	GGCTCCCACA	GCTCTGGCGA	CGGCGCTTGA	CGTGGGCTTG	300
	TCCAACTGGA	GCTTCCTGTA	TGTCACCGTC	TCGCTGTACA	CAATGACCAA	ATCCTCAGCT	360
	GTCCTCTTCA	TCTTGATCTT	CTCTCTGATC	TTCAAGCTGG	AGGAGCTGCG	CGCGGCACTG	420
10	GTCCTGGTGG	TCCTCCTCAT	CGCCGGGGGT	CTCTTCATGT	TCACCTACAA	GTCCACACAG	480
	TTCAACGTGG	AGGGCTTCGC	CTTGGTGCTG	GGGGCCTCGT	TCATCGGTGG	CATTCGCTGG	540
•	ACCCTCACCC	AGATGCTCCT	GCAGAAGGCT	GAACTCGGCC	TCCAGAATCC	CATCGACACC	600
	ATGTTCCACC	TGCAGCCACT	CATGTTCCTG	GGGCTCTTCC	CTCTCTTTGC	TGTATTTGAA	660
	GGTCTCCATT	TGTCCACATC	TGAGAAAATC	TTCCGTTTCC	AGGACACAGG	GCTGCTCCTG	720
15	CGGGTACTTG	GGAGCCTCTT	CCTTGGCGGG	ATTCTCGCCT	TTGGTTTGGG	CTTCTCTGAG	780
	TTCCTCCTGG	TCTCCAGAAC	CTCCAGCCTC	ACTCTCTCCA	TTGCCGGCAT	TTTTAAGGAA	840
	GTCTGCACTT	TGCTGTTGGC	AGCTCATCTG	CTGGGCGATC	AGATCAGCCT	CCTGAACTGG	900
	CTGGGCTTCG	CCCTCTGCCT	CTCGGGAATA	TCCCTCCACG	TTGCCCTCAA	AGCCCTGCAT	960
	TCCAGAGGTG	ATGGTGGCCC	CAAGGCCTTG	AAGGGGCTGG	GCTCCAGCCC	CGACCTGGAG	1020
20	CTGCTGCTCC	GGAGCAGCCA	GCGGGAGGAA	GGTGACAATG	AGGAGGAGGA	GTACTTTGTG	1080
	GCCCAGGGGC	AGCAG					1095

(2) INFORMATION FOR SEQ ID NO: 33:

- 25 (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 678
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
- 30 (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- (B) CELL KIND: Stomach cancer
- 35 (D) CLONE NAME: HP10429
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 33:

117

	ATGCCTACCA	CAAAGAAGAC	ATTGATGTTC	TTATCAAGCT	TTTTCACCAG	CCTTGGGTCC	60
	TTCATTGTAA	TTTGCTCTAT	TCTTGGGACA	CAAGCATGGA	TCACCAGTAC	AATTGCTGTT	120
	AGAGACTCTG	CTTCAAATGG	GAGCATTTTC	ATCACTTACG	GACTTTTTCG	TGGGGAGAGT	180
	AGTGAAGAAT	TGAGTCACGG	ACTTGCAGAA	CCAAAGAAAA	AGTTTGCAGT	TTTAGAGATA	240
5	CTGAATAATT	CTTCCCAAAA	AACTCTGCAT	TCGGTGACTA	TCCTGTTCCT	GGTCCTGAGT	300
	TTGATCACGT	CGCTGCTGAG	CTCTGGGTTT	ACCTTCTACA	ACAGCATCAG	CAACCCTTAC	360
	CAGACATTCC	TGGGGCCGAC	GGGGGTGTAC	ACCTGGAACG	GGCTCGGTGC	ATCCTTCGTT	420
	TTTGTGACCA	TGATACTGTT	TGTGGCGAAC	ACGCAGTCCA	ACCAACTCTC	CGAAGAGTTG	480
	TTCCAAATGC	TTTACCCGGC	AACCACCAGT	AAAGGAACGA	CCCACAGTTA	CGGATACTCG	540
10	TTCTGGCTCA	TACTGCTCGT	CATTCTTCTA	AATATAGTCA	CTGTAACCAT	CATCATTTTC	600
	TACCAGAAGG	CCAGATACCA	GCGGAAGCAG	GAGCAGAGAA	AGCCAATGGA	ATATGCTCCA	660
	AGGGACGGAA	TTTTATTC					678

15 (2) INFORMATION FOR SEQ ID NO: 34:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 387
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 20 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

- (A) ORGANISM: Homo sapiens
- 25 (B) CELL KIND: Liver
 - (D) CLONE NAME: HP10432

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 34:

	(2) INFORMATION FOR SEQ ID NO: 35:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 489	
	(B) TYPE: Nucleic acid	
5	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
10	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Liver	
	(D) CLONE NAME: HP10433	
<u>.</u> _	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 35:	
15		
	ATGCGACGGC TGCTGATCCC TCTGGCCCTG TGGCTGGGCG CGGTGGGCGT GGGCGTCGCC	60
	GAGCTCACGG AAGCCCAGCG CCGGGGCCTG CAGGTGGCCC TGGAGGAATT TCACAAGCAC	120
	CCGCCCGTGC AGTGGGCCTT CCAGGAGACC AGTGTGGAGA GCGCCGTGGA CACGCCCTTC	180
	CCAGCTGGAA TATTTGTGAG GCTGGAATTT AAGCTGCAGC AGACAAGCTG CCGGAAGAGG	240
20	GACTGGAAGA AACCCGAGTG CAAAGTCAGG CCCAATGGGA GGAAACGGAA ATGCCTGGCC	300
	TGCATCAAAC TGGGCTCTGA GGACAAAGTT CTGGGCCGGT TGGTCCACTG CCCCATAGAG	360
	ACCCAAGTTC TGCGGGAGGC TGAGGAGCAC CAGGAGACCC AGTGCCTCAG GGTGCAGCGG	420
	GCTGGTGAGG ACCCCCACAG CTTCTACTTC CCTGGACAGT TCGCCTTCTC CAAGGCCCTG	480
25	CCCCGCAGC	489
2.5		
	(2) INFORMATION FOR SEQ ID NO: 36:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 579	
30	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
35	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10480	

119

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 36:

	ATGATCCGCT GCGGCCTGGC CTGCGAGCGC TGCCGCTGGA TCCTGCCCCT GCTCCTACTC	60
	AGCGCCATCG CCTTCGACAT CATCGCGCTG GCCGGCCGCG GCTGGTTGCA GTCTAGCGAC	120
5	CACGGCCAGA CGTCCTCGCT GTGGTGGAAA TGCTCCCAAG AGGGCGGCGG CAGCGGGTCC	180
	TACGAGGAGG GCTGTCAGAG CCTCATGGAG TACGCGTGGG GTAGAGCAGC GGCTGCCATG	240
	CTCTTCTGTG GCTTCATCAT CCTGGTGATC TGTTTCATCC TCTCCTTCTT CGCCCTCTGT	300
	GGACCCCAGA TGCTTGTCTT CCTGAGAGTG ATTGGAGGTC TCCTTGCCTT GGCTGCTGTG	360
	TTCCAGATCA TCTCCCTGGT AATTTACCCC GTGAAGTACA CCCAGACCTT CACCCTTCAT	420
10	GCCAACCGTG CTGTCACTTA CATCTATAAC TGGGCCTACG GCTTTGGGTG GGCAGCCACG	480
	ATTATCCTGA TCGGCTGTGC CTTCTTCTTC TGCTGCCTCC CCAACTACGA AGATGACCTT	540
	CTGGGCAATG CCAAGCCCAG GTACTTCTAC ACATCTGCC	579
15	(2) INFORMATION FOR SEQ ID NO: 37:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1502	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
20	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	() ORIGINAL COMPON	
	(vi) ORIGINAL SOURCE:	
25	(A) ORGANISM: Homo sapiens (B) CELL KIND: Liver	
23	(D) CLONE NAME: HP01263	
	(D) CLONE NAME: HPU1203	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
30	(B) EXISTENCE POSITION: 37 1185	
	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 37:	
35	ACAAACTGAC CCATCCTGGG CCTTGTTCTC CACAGA ATG GGT CTG CTC CTT CCC	54
	Met Gly Leu Leu Pro	
	1 5	
	CTG GCA CTC TGC ATC CTA GTC CTG TGC TGC GGA GCA ATG TCT CCA CCC	102

	Leu	Ala	Leu	Cys	Ile	Leu	Val	Leu	Cys	Cys	Gly	Ala	Met	Ser	Pro	Pro	
				10					15					20			
	CAG	CTG	GCC	CTC	AAC	CCC	TCG	GCT	CTG	CTC	TCC	CGG	GGC	TGC	AAT	GAC	150
	Gln	Leu	Ala	Leu	Asn	Pro	Ser	Ala	Leu	Leu	Ser	Arg	Gly	Cys	Asn	Asp	
5			25					30					35				
	TCC	GAT	GTG	CTG	GCA	GTT	GCA	GGC	TTT	GCC	CTG	CGG	GAT	ATT	AAC	AAA	198
	Ser	Asp	Val	Leu	Ala	Val	Ala	Gly	Phe	Ala	Leu	Arg	Asp	Ile	Asn	Lys	
		40					45					50					
	GAC	AGA	AAG	GAT	GGC	TAT	GTG	CTG	AGA	CTC	AAC	CGA	GTG	AAC	GAC	GCC	246
10	Asp	Arg	Lys	Asp	Gly	Tyr	Val	Leu	Arg	Leu	Asn	Arg	Val	Asn	Asp	Ala	
	55					60					65	•				70	
						GGT											294
	Gln	Glu	Tyr	Arg	Arg	Gly	Gly	Leu	Gly	Ser	Leu	Phe	Tyr	Leu	Thr	Leu	
					75					80					85	•	
15						GAC											342
	Asp	Val	Leu		Thr	Asp	Cys	His		Leu	Arg	Lys	Lys	Ala	Trp	Gln	
				90					95					100			
						ATA											390
20	Asp	Cys		Met	Arg	Ile	Phe		Glu	Ser	Val	Tyr	_	Gln	Cys	Lys	
20	CCA	A T' A	105	ጥልጥ	A TPC	440	4.4.0	110	4 C TT	404	0 mm	0.00	115	mm 4	00m	CCT	
	•					AAC Asn											438
	win	120	1 116	1,11	Het	Veir	125	FLO	ser	urg	AST	130	ıyı	Leu	NIG	AIA	
	TAT		ፐርፐ	ACT	СТТ	CGC		СТТ	TCA	A A A	ΔΔΔ		Δ T T	TAC	ልጥር	ACG	486
25						Arg											400
	135		٠,٠		Beu	140	110	,,,	DC1	<i>D</i> , 3	145	шуз	110	1,1		150	
		ССТ	GAC	TGC	CCA	AGC	TCC	АТА	CCC	АСТ		тст	TCC	ААТ	CAC		534
						Ser											
				-,-	155					160	ш				165		
30	GTG	CTG	GAG	GCT	GCC	ACC	GAG	TCT	CTT		AAA	TAC	AAC	AAT		AAC	582
						Thr											
				170					175		•	•		180			
	ACA	TCC	AAG	CAG	TAT	TCT	CTC	TTC	AAA	GTC	ACC	AGG	GCT	TCT	AGC	CAG	630
	Thr	Ser	Lys	Gln	Tyr	Ser	Leu	Phe	Lys	Val	Thr	Arg	Ala	Ser	Ser	Gln	
35			185					190	·				195				
	TGG	GTG	GTC	GGC	CCT	TCT	TAC	TTT	GTG	GAA	TAC	TTA	ATT	AAA	GAA	TCA	678
						Ser											
		200					205				,	210					

	215 TCT		Thr	Lys	Ser	Gln	Ala	Ser	Ser	Cys	Ser	Leu	Gln	Ser	Ser	Asp	
	TCT	C TI C														•	
		ORO				220					225					230	
	_	GIG	CCT	GTT	GGT	CTT	TGC	AAA	GGT	TCT	CTG	ACT	CGA	ACA	CAC	TGG	774
5	Ser	Val	Pro	Val	Gly	Leu	Cys	Lys	G1y	Ser	Leu	Thr	Arg	Thr	His	Trp	
					235					240					245		
	GAA	AAG	TTT	GTC	TCT	GTG	ACT	TGT	GAC	TTC	TTT	GAA	TCA	CAG	GCT	CCA	822
	Glu	Lys	Phe	Val	Ser	Val	Thr	Cys	Asp	Phe	Phe	Glu	Ser	G1n	Ala	Pro	
				250					255					260			
10	GCC	ACT	GGA	AGT	GAA	AAC	TCT	GCT	GTT	AAC	CAG	AAA	CCT	ACA	AAC	CTT	870
	Ala	Thr	Gly	Ser	Glu	Asn	Ser	Ala	Val	Asn	Gln	Lys	Pro	Thr	Asn	Leu	
			265					270					275				
													CCA				918
	Pro	Lys	Val	Glu	Glu	Ser	Gln	Gln	Lys	Asn	Thr	Pro	Pro	Thr	Asp	Ser	
15		280					285					290					
													CTT				966
		Ser	Lys	Ala	Gly	Pro	Arg	Gly	Ser	Val	Gln	Tyr	Leu	Pro	Asp	Leu	
	295					300					305					310	
00													GCC				1014
20	Asp	Asp	Lys	Asn		Gln	G1u	Lys	Gly	Pro	Gln	Glu	Ala	Phe	Pro	Val	
					315					320					325		
													CTG				1062
	HIS	Leu	Asp	_	Thr	Thr	Asn	Pro		Gly	Glu	Thr	Leu	Asp	Ile	Ser	
25	mm c	C.II.O.	mmo.	330					335					340			
25													GTC				1110
	Pne	reu		Leu	Glu	Pro	Met		Glu	Lys	Leu	Val	Val	Leu	Pro	Phe	
	ccc	A A A	345	A A A	CC4	cco	4.C/M	350		m 00			355				
													CCA				1158
30	110	360	GIU	гуз	VIA	Arg		AIA	GIU	Cys	Pro		Pro	ATB	GIn	Asn	
J 0	GCC		ርርም	CTT	CTC	ርጥጥ	365	CC4	TO A C	• A A MC		370	\G TC1	.m. 0#	70 M 4 C		
			Pro						IGAG	MAIC	AC A	MOAGA	1G1C1	T CI	GIAG	166	1210
	375	201	110	Deu	Val	380	110	rio									
		rggte	ece c	CGCA	TCAC		CC AC	CCC4	ጥርር	ירר אר	ጥልጥ	CCAC	. 4 C 4 C	۰۸۲ ۸		GTGCA	1170
35																TGACT	1270 1330
																ACTGC	1390
																ATGCC	
		TTAT														MIGCC	1450

	(2) INFORMATION FOR SEQ ID NO: 38:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1349	
5	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
•		
10	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
•	(B) CELL KIND: Liver	
	(D) CLONE NAME: HP01299	
15	·	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 111 1064	
	(C) CHARACTERIZATION METHOD: E	
20		
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 38:	
	AGCAGTTGGG GCAGGAGGAA GCCGACTGCT GCCTGGTCTG CAAAGAAGTC CTTTCAAGTC	60
25	TCTAGGACTG GACTCTTCCT AAGCAAGTCC GAGAAGGAAG CACCCTCACT ATG TGG	116
25	Met Trp	
	1	
	CTC TAC CTG GCG GCC TTC GTG GGC CTG TAC TAC CTT CTG CAC TGG TAC	
30	Leu Tyr Leu Ala Ala Phe Val Gly Leu Tyr Tyr Leu Leu His Trp Tyr	
30	5 10 15	010
	CGG GAG AGG CAG GTG GTG AGC CAC CTC CAA GAC AAG TAT GTC TTT ATC Arg Glu Arg Gln Val Val Ser His Leu Gln Asp Lys Tyr Val Phe Ile	212
	20 25 30	
	ACG GGC TGT GAC TCG GGC TTT GGG AAC CTG CTG GCC AGA CAG CTG GAT	260
35	Thr Gly Cys Asp Ser Gly Phe Gly Asn Leu Leu Ala Arg Gln Leu Asp	260
	35 40 45 50	
	GCA CGA GGC TTG AGA GTG CTG GCT GCG TGT CTG ACG GAG AAG GGG GCC	308
	Ala Arg Gly Leu Arg Val Leu Ala Ala Cys Leu Thr Glu Lys Gly Ala	200
	or bea me far bea are are cys fed the gra by or and	

					55					60					65		
	GAG	CAG	CTG	AGG	GGC	CAG	ACG	TCT	GAC	AGG	CTG	GAG	ACG	GTG	ACC	CTG	356
	Glu	Gln	Leu	Arg	Gly	Gln	Thr	Ser	Asp	Arg	Leu	Glu	Thr	Val	Thr	Leu	
				70					75					80			
5	GAT	GTT	ACC	AAG	ATG	GAG	AGC	ATC	GCT	GCA	GCT	ACT	CAG	TGG	GTG	AAG	404
	Asp	Val	Thr	Lys	Met	Glu	Ser	Ile	Ala	Ala	Ala	Thr	Gln	Trp	Val	Lys	
			85					90					95				
	GAG	CAT	GTG	GGG	GAC	AGA	GGA	CTC	TGG	GGA	CTG	GTG	AAC	AAT	GCA	GGC	452
	Glu	His	Val	Gly	Asp	Arg	Gly	Leu	Trp	Gly	Leu	Val	Asn	Asn	Ala	Gly	
10		100					105	•				110					
	ATT	CTT	ACA	CCA	ATT	ACC	TTA	TGT	GAG	TGG	CTG	AAC	ACT	GAG	GAC	TCT	500
	Ile	Leu	Thr	Pro	Ile	Thr	Leu	Cys	Glu	Trp	Leu	Asn	Thr	Glu	Asp	Ser	
	115					120					125					130	
	ATG	AAT	ATG	CTC	AAA	GTG	AAC	CTC	ATT	GGT	GTG	ATC	CAG	GTG	ACC	TTG	548
15	Met	Asn	Met	Leu	Lys	Val	Asn	Leu	Ile	Gly	Val	Ile	Gln	Va1	Thr	Leu	
					135					140					145		
	AGC	ATG	CTT	CCT	TTG	GTG	AGG	AGA	GCA	CGG	GGA	AGA	ATT	GTC	AAT	GTC	596
	Ser	Met	Leu	Pro	Leu	Val	Arg	Arg	Ala	Arg	Gly	Arg	Ile	Val	Asn	Val	
				150					155					160			
20			ATT														644
	Ser	Ser	Ile	Leu	Gly	Arg	Val	Ala	Phe	Phe	Va1	Gly	Gly	Tyr	Cys	Val	
			165					170					175				
			TAT														692
	Ser	Lys	Tyr	Gly	Val	Glu	Ala	Phe	Ser	Asp	Ile	Leu	Arg	Arg	Glu	Ile	
25	٥	180					185					190					
			TTT														740
		His	Phe	Gly	Val	Lys	Ile	Ser	Ile	Val	Glu	Pro	Gly	Tyr	Phe	Arg	
	195					200					205					210	
			ATG														788
30	Thr	Gly	Met	Thr		Met	Thr	Gln	Ser		Glu	Arg	Met	Lys		Ser	
					215					220					225		
			GAA														836
	Trp	Lys	Glu		Pro	Lys	His	Ile		Glu	Thr	Tyr	Gly	Gln	Gln	Tyr	
2 -				230					235					240			
35			GCC														884
	rne	ASP	Ala	Leu	Tyr	Asn	He		Lys	Glu	Gly	Leu		Asn	Cys	Ser	
	464		245					250					255				
	AUA	AAC	CTG	AAC	CTG	GTC	ACT	GAC	TGC	ATG	GAA	CAT	GCT	CTG	ACA	TCG	932

124																	
	Thr	Asn	Leu	Asn	Leu	Val	Thr	Asp	Cys	Met	Glu	His	Ala	Leu	Thr	Ser	
		260					265					270					
	GTG	CAT	CCG	CGA	ACT	CGA	TAT	TCA	GCT	GGC	TGG	GAT	GCT	AAA	TTT	TTC	980
	Val	His	Pro	Arg	Thr	Arg	Tyr	Ser	Ala	Gly	Trp	Asp	Ala	Lys	Phe	Phe	
5	275					280					285					290	
	TTC	ATC	CCT	CTA	TCT	TAT	TTA	CCT	ACA	TCA	CTG	GCA	GAC	TAC	ATT	TŤG	1028
	Phe	Ile	Pro	Leu	Ser	Tyr	Leu	Pro	Thr	Ser	Leu	Ala	Asp	Tyr	Ile	Leu	
					295		•			300					305		
	ACT	AGA	TCT	TGG	CCC	AAA	CCA	GCC	CAG	GCA	GTC	TAA	AGAA	AAC	TGGG	TTGGT	1080
LO	Thr	Arg	Ser	Trp	Pro	Lys	Pro	Ala	Gln	Ala	Val						
•				310					315								
	GCT'	CTT	GGA A	ATGA	AGGC	AA AA	ATC:	TGAA	A TT	GTTAC	STGT	CTC	AGTA	ATC (CTGA	TTTAGA	1140
	ACC	CAGG	CTT :	rttg:	PAAC	AA T	TGT:	TTTC:	T TG	CCTA	AATT	CAT'	TAT	CTG	GCAT	CATCAG	1200
	AGT	ACTA	ACA :	rgtt:	'ATA	rt to	CAGA!	TATC	C AA	AGCT:	DOAT	ACT'	LTA G(GTG .	ATGA.	ATCTTT	1260
L 5	ACT	ATTT'	TAG (CCCT	rttt:	rg a'	rgag.	ACTA:	T TT	GTCT	AAAG	TGA	ATCA'	TTT (GTTC	TTGCCT	1320
	TAT	TAAA	CAG	AGTA	GATG	GA A	AACA	ATTT									1349
	(2)	INF	ORMA'	TION	FOR	SEQ	ID I	NO: :	39:								
20		(:	i) S	EQUE	NCE (CHAR	ACTE	RIST	ics:								
				(A)	LEN	GTH:	164	3									
				(B)	TYP	E: N	ıcle:	ic a	cid								
					o mn												

- - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
- 25 (ii) SEQUENCE KIND: cDNA to mRNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Liver
- 30 (D) CLONE NAME: HP01347
 - (ix) SEQUENCE CHARACTERISTICS:
 - (A) CHARACTERIZATION CODE: CDS
 - (B) EXISTENCE POSITION: 25.. 915
- 35 (C) CHARACTERIZATION METHOD: E
 - (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 39:

	AACA	ATCT	GG (ACAC	CGGC	SA A	AAC A	ATG A	AGT	GAC '	rcc .	AAG (GAA (CCA	AGG (GTG	51
							1	let :	Ser .	Asp :	Ser	Lys (Glu 🕽	Pro A	Arg '	Val	
		•		•				1				5					
	CAG	CAG	CTG	GGC	CTC	CTG	GGG	TGT	CTT	GGC	CAT	GGC	GCC	CTG	GTG	CTG	99
5	Gln	Gln	Leu	Gly	Leu	Leu	Gly	Cys	Leu	Gly	His	Gly	Ala	Leu	Val	Leu	
	10					15					20					25	
	CAA	CTC	CTC	TCC	TTC	ATG	CTC	TTG	GCT	GGG	GTC	CTG	GTG	GCC	ATC	CTT	147
	Gln	Leu	Leu	Ser	Phe	Met	Leu	Leu	Ala	Gly	Val	Leu	Val	Ala	Ile	Leu	
					30					35					40		
10	GTC	CAA	GTG	TCC	AAG	GTC	CCC	AGC	TCC	CTA	AGT	CAG	GAA	CAA	TCC	GAG	195
	Va1	Gln	Val	Ser	Lys	Val	Pro	Ser	Ser	Leu	Ser	Gln	Glu	Gln	Ser	Glu	
				45				•	50					55			
	CAA	GAC	GCA	ATC	TAC	CAG	AAC	CTG	ACC	CAG	CTT	AAA	GCT	GCA	GTG	GGT	243
	Gln	Asp	Ala	Ile	Tyr	Gln	Asn	Leu	Thr	Gln	Leu	Lys	Ala	Ala	Val	Gly	
15			60					65					70				
	GAG	CTC	TCA	GAG	AAA	TCC	AAG	CTG	CAG	GAG	ATC	TAC	CAG	GAG	CTG	ACC	291
	Glu	Leu	Ser	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	G1u	Leu	Thr	
		75					80					85					
	CAG	CTG	AAG	GCT	GCA	GTG	GGT	GAG	TTG	CCA	GAG	AAA	TCC	AAG	CTG	CAG	339
20	Gln	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	G1n	
	90					95					100					105	
	GAG	ATC	TAC	CAG	GAG	CTG	ACC	CGG	CTG	AAG	GCT	GCA	GTG	GGT	GAG	TTG	387
	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	Arg	Leu	Lys	Ala	-Ala	Val	Gly	Glu	Leu	
					110					115					120		
25	CCA	GAG	AAA	TCC	AAG	CTG	CAG	GAG	ATC	TAC	CAG	GAG	CTG	ACC	CGG	CTG	435
	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	Arg	Leu	
				125					130					135			
	AAG	GCT	GCA	GTG	GGT	GAG	TTG	CCA	GAG	AAA	TCC	AAG	CTG	CAG	GAG	ATC	483
	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	
30			140					145					150				
	TAC	CAG	GAG	CTG	ACC	CGG	CTG	AAG	GCT	GCA	GTG	GGT	GAG	TTG	CCA	GAG	531
	Tyr	Gln	Glu	Leu	Thr	Arg	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Glu	
		155					160					165					
	AAA	TCC	AAG	CTG	CAG	GAG	ATC	TAC	CAG	GAG	CTG	ACG	GAG	CTG	AAG	GCT	579
35	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	Glu	Leu	Thr	Glu	Leu	Lys	Ala	
	170					175					180					185	
	GCA	GTG	GGT	GAG	TTG	CCA	GAG	AAA	TCC	AAG	CTG	CAG	GAG	ATC	TAC	CAG	627
	Ala	Val	Gly	Glu	Leu	Pro	Glu	Lys	Ser	Lys	Leu	Gln	Glu	Ile	Tyr	Gln	

· 126

					190					195					200		
	GAG	CTG	ACC	CAG	CTG	AAG	GCT	GCA	GTG	GGT	GAG	TTG	CCA	GAC	CAG	TCC	675
	Glu	Leu	Thr	Gln	Leu	Lys	Ala	Ala	Val	Gly	Glu	Leu	Pro	Asp	G1n	Ser	
				205					210					215			
5	AAG	CAG	CAG	CAA	ATC	TAT	CAA	GAA	CTG	ACC	GAT	TTG	AAG	ACT	GCA	TTT	723
	Lys	Gln	Gln	Gln	Ile	Tyr	Gln	Glu	Leu	Thr	Asp	Leu	Lys	Thr	Ala	Phe	
			220					225					230				
	GAA	CGC	CTG	TGC	CGC	CAC	TGT	CCC	AAG	GAC	TGG	ACA	TTC	TTC	CAA	GGA	771
	Glu	Arg	Leu	Cys	Arg	His	Cys	Pro	Lys	Asp	Trp	Thr	Phe	Phe	Gln	Gly	
10		235					240					245					
	AAC	TGT	TAC	TTC	ATG	TCT	AAC	TCC	CAG	CGG	AAC	TGG	CAC	GAC	TCC	GTC	819
	Asn	Cys	Tyr	Phe	Met	Ser	Asn	Ser	Gln	Arg	Asn	Trp	His	Asp	Ser	Val	
	250					255					260					265	
	ACC	GCC	TGC	CAG	GAA	GTG	AGG	GCC	CAG	CTC	GTC	GTA	ATC	AAA	ACT	GCT	867
15	Thr	Ala	Cys	Gln	Glu	Val	Arg	Ala	Gln	Leu	Val	Val	Ile	Lys	Thr	Ala	
					270					275					280		
	GAG	GAG	CAG	CTT	CCA	GCG	GTA	CTG	GAA	CAG	TGG	AGA	ACC	CAA	CAA		912
	Glu	Glu	G1n	Leu	Pro	Ala	Val	Leu	Glu	Gln	Trp	Arg	Thr	Gln	Gln		
				285					290					295			
20	TAG	CGGG	AAT (GAAGA	ACTG	rg co	GGAA')ATT1	TG	CAG	rggc	TGG	AACG/	ACA A	ATCG/	ATGT	970
	GAC	GTTG.	ACA A	ATTA	CTGG	AT C	TGCA/	AAAA	G CC	CGCAC	CCT	GCT	rcag/	AGA (CGAA1	TAGTTG	1030
																AAGCCA	1090
	GCG	CTTC	TTC '	TCTC	CATC	CT TO	GGAC	CTTC	A CA	AATGO	CCCT	GAGA	ACGG	rtc :	rctg1	TTCGAT	1150
																CCCTG	1210
25																GATGC	1270
																SATTAG	1330
	ACT	ATTT	GGA '	TŢCA'	rgtg:	ra G	CTGC	CCTG	r cc	CCTGC	GGC	TTTA	ATCT	CAT	CCATO	CAAAC	1390
																CTGGT	1450
															•	ACCAAT	1510
30																CTTTG	1570
					rcca'	r T T	GGCT(STTT(C TG	AGTTO	TAG	CCT	TATA	AAT A	AAAG1	TGGTAA	1630
	ATG:	TTGT.	AAC 1	TGC													1643

35 (2) INFORMATION FOR SEQ ID NO: 40:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 729
 - (B) TYPE: Nucleic acid

	(C) STRANDEDNESS	S: Double		
	(D) TOPOLOGY: L	inear		
	(ii) SEQ	UENCE KIND: cl	ONA to mRNA		
5	(vi) ORI	GINAL SOURCE:		•	
) ORGANISM: H	•		
	(B) CELL KIND: S	Stomach cance	er	
	(D) CLONE NAME:	HP01440		
10	(i-) CEO		TO T		
10	_	UENCE CHARACTI		200	
) CHARACTERIZA) EXISTENCE PO			
) CHARACTERIZA			
	(0	, omnasormer	TION HEIMOD	. ь	
15	(xi) SEQ	UENCE DESCRIP	TION: SEO ID	NO: 40:	
	• , •				
	ACTTTCACTC ACC	SCCTGTC CTTCC	TGACA CCTCACO	C ATG TGT ACG GGA AAA TGT	r 55
				Met Cys Thr Gly Lys Cys	3
				1 5	
20	GCC CGC TGT GT	G GGG CTC TCC	CTC ATT ACC	CTC TGC CTC GTC TGC ATT	103
	Ala Arg Cys Va	l Gly Leu Ser	Leu Ile Thr	Leu Cys Leu Val Cys Ile	
	10		15	20	
	GTG GCC AAC GC	C CTC CTG CTG	GTA CCT AAT	GGG GAG ACC TCC TGG ACC	151
	Val Ala Asn Ala	a Leu Leu Leu	Val Pro Asn	Gly Glu Thr Ser Trp Thr	
25	25		30	35	
				CTC ATG GGC GGC TTC ATT	199
			Gln Val Trp	Leu Met Gly Gly Phe Ile	
	40	45		50	
20				ATT GCA GCC GTT CGG GCA	247
30			Cys Pro Gly	Ile Ala Ala Val Arg Ala	
	55	60	CCT CCC TCC	65 70	205
				TGT GGA AAC CGC TGC AGG	295
	GIY GIY LYS GI	y cys cys 61y 75	80	Cys Gly Asn Arg Cys Arg 85	
35	ATG CTG CGC TC			GGG GTG CTT GGT GCC ATC	343
				Gly Val Leu Gly Ala Ile	343
	9		95	100	
				CGA AAT GGA CCC AGA TGC	391

Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu Arg Asn Gly Pro Arg Cys												
	Tyr Cys Leu Ser Val Ser Gly Ala Gly Leu Arg Asn Gly Pro Arg	Cys										
	105 110 115											
	TTA ATG AAC GGC GAG TGG GGC TAC CAC TTC GAA GAC ACC GCG GGA	GCT 439										
	Leu Met Asn Gly Glu Trp Gly Tyr His Phe Glu Asp Thr Ala Gly	Ala										
5	120 125 130											
	TAC TTG CTC AAC CGC ACT CTA TGG GAT CGG TGC GAG GCG CCC CCT	CGC 487										
	Tyr Leu Leu Asn Arg Thr Leu Trp Asp Arg Cys Glu Ala Pro Pro	Arg										
	135 140 145	150										
	GTG GTC CCC TGG AAT GTG ACG CTC TTC TCG CTG CTG GCC GCC	TCC 535										
10	Val Val Pro Trp Asn Val Thr Leu Phe Ser Leu Leu Val Ala Ala	Ser										
	155 160 165											
	TGC CTG GAG ATA GTA CTG TGT GGG ATC CAG CTG GTG AAC GCG ACC	ATT 583										
	Cys Leu Glu Ile Val Leu Cys Gly Ile Gln Leu Val Asn Ala Thr	Ile										
	170 175 180											
15	GGT GTC TTC TGC GGC GAT TGC AGG AAA AAA CAG GAC ACC CCT CAC	TG 630										
	Gly Val Phe Cys Gly Asp Cys Arg Lys Lys Gln Asp Thr Pro His											
	185 190 195											
	AGGCTCCACT GACCGCCGGG TTACACCTGC TCCTTCCTGG ACGCCTACCT GGCTC	GCTCA 690										
	CTCCCTTGCT CGCTAGAATA AACTGCTTTG CGCTCTCTT	729										
20												
	(2) INFORMATION FOR SEQ ID NO: 41:											
	(i) SEQUENCE CHARACTERISTICS:											
	(A) LENGTH: 1322											
25	(B) TYPE: Nucleic acid											
	(C) STRANDEDNESS: Double											
	(D) TOPOLOGY: Linear											
	(ii) SEQUENCE KIND: cDNA to mRNA											
30	(vi) ORIGINAL SOURCE:											
	(A) ORGANISM: Homo sapiens											
	(B) CELL KIND: Stomach cancer											
	(D) CLONE NAME: HP01526											
35	(ix) SEQUENCE CHARACTERISTICS:											
	(A) CHARACTERIZATION CODE: CDS											
	(B) EXISTENCE POSITION: 84 749											
	(C) CHARACTERIZATION METHOD: E											

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 41:

	GAG	CGC	AGG '	TCTG	GCT	GC AC	TAG	STCC	C GG(CAAC	CGCA	GG	CTCGC	GGC	GGG	CGC	TGGG	60
	CGCC	GGA	rcc (GACT	CTAG	rc g	ra at	rg ga	AG G	CG G	GC G	GC '	TTT C	TG (GAC	TCG	CTC	113
5							Me	et G	lu A	La G	ly G	ly !	Phe L	eu A	Asp	Ser	Leu	
								1				5					10	
	ATT	TAC	GGA	GCA	TGC	GTG	GTC	TTC	ACC	CTT	GGC	AT	G TTC	TC	C GC	C G	GC	161
	Ile	Tyr	Gly	Ala	Ċys	Val	Va1	Phe	Thr	Leu	Gly	Me	t Phe	Sei	r Al	a G	ly	
	•				15					20					2	5		
10	CTC	TCG	GAC	CTC	AGG	CAC	ATG	CGA	ATG	ACC	CGG	AG	T GTG	GAO	CAA	C G	TC	209
	Leu	Ser	Asp	Leu	Arg	His	Met	Arg	Met	Thr	Arg	Se	r Val	Asj	p As	n V	al	
				30					35					40	0			
													C CTG					257
	Gln	Phe	Leu	Pro	Phe	Leu	Thr	Thr	Glu	Val	Asn	Ası	n Leu	Gly	y Tr	p L	eu	
15			45					50					55					
													C GTC					305
	Ser		Gly	Ala	Leu	Lys	Gly	Asp	Gly	Ile	Leu	Il	e Val	Va]	l As	n T	hr	
		60					65					70						
													A TAT					353
20	Val	Gly	Ala	Ala	Leu	Gln	Thr	Leu	Tyr	Ile	Leu	Ala	a Tyr	Lei	ı Hi	s T	yr	
	75					80					85						90	
													A ACC					401
	Суѕ	Pro	Arg	Lys	Arg	Val	Val	Leu	Leu	Gln	Thr	Ala	a Thr	Lei	ı Le	u G	ly	
					95					100					10			
25													G GTA					449
	Val	Leu	Leu	Leu	Gly	Tyr	Gly	Tyr	Phe	Trp	Leu	Lei	u Val	Pro	As	n P	ro	
				110					115					120				
													T GTC					497
	Glu	Ala		Leu	Gln	Gln	Leu	Gly	Leu	Phe	Cys	Se	r Val	Phe	e Th	r I	le	
30			125					130					135					
							•						G GTG					545
	Ser	Met	Tyr	Leu	Ser	Pro	Leu	Ala	Asp	Leu	Ala	Ly	s Val	Ιle	e Gl	n T	hr	
		140					145					15	0					
	AAA	TCA	ACC	CAA	TGT	CTC	TCC	TAC	CCA	CTC	ACC	AT	T GCT	ACC	с ст	T C	TC	593
35	Lys	Ser	Thr	Gln	Cys	Leu	Ser	Tyr	Pro	Leu	Thr	110	e Ala	Thi	c Le	u L	eu	
	155					160					165					1	70	
	ACC	TCT	GCC	TCC	TGG	TGC	CTC	TAT	GGG	TTT	CGA	CT	C AGA	GAT	r cc	C T	AT	641
	Thr	Ser	Ala	Ser	Trp	Cys	Leu	Tyr	Gly	Phe	Arg	Le	u Arg	Ası	p Pr	o T	yr	

130

	175 180 185	
	ATC ATG GTG TCC AAC TTT CCA GGA ATC GTC ACC AGC TTT ATC CGC TTC	689
	Ile Met Val Ser Asn Phe Pro Gly Ile Val Thr Ser Phe Ile Arg Phe	
	190 195 200	
5	TGG CTT TTC TGG AAG TAC CCC CAG GAG CAA GAC AGG AAC TAC TGG CTC	737
	Trp Leu Phe Trp Lys Tyr Pro Gln Glu Gln Asp Arg Asn Tyr Trp Leu	
	205 210 215	
	CTG CAA ACC TGAGGCTGCT CATCTGACCA CTGGGCACCT TAGTGCCAAC CTGA	790
	Leu Gln Thr	
10	220	
	ACCAAAGAGA CCTCCTTGTT TCAGCTGGGC CTGCTGTCCA GCTTCCCAGG TGCAGTGGGT	850
	TGTGGGAACA AGAGATGACT TTGAGGATAA AAGGACCAAA GAAAAAGCTT TACTTAGATG	910
	ATTGATTGGG GCCTAGGAGA TGAAATCACT TTTTATTTTT TAGAGATTTT TTTTTTTAAT	970
	TTTGGAGGTT GGGGTGCAAT CTTTAGAATA TGCCTTAAAA GGCCGGCCGC GGTGGCTCAC	1030
15	GCCTGTAATC CCAGCACTTT GGGAGGCCAA GGTGGGCGGA TCGCCTGAGG TCAGGAGTTC	1090
	AAGACCAACC TGACTAACAT GGTGAAACCC CATCTCTACT AAAAATACAA AATTAGCCAG	1150
	GCATGATGGC ACATGCCTGT AATCCCAGAT ACTTGGGAGG CTGAGGCAGG AGAATTGCTT	1210
	GAACCCAGGA GGTGGAGGTT GCAGTGAGCT GAGATCGTGC CATTGTGATA TGAATATGCC	1270
	TTATATGCTG ATATGAATAT GCCTTAAAAT AAAGTGTTCC CCACCCCTGC CC	1322
20		
	(2) INFORMATION FOR SEQ ID NO: 42:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 3045	
25	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
2.0		
30	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10230	
35	(im) CEOUTINGE CHADACTER TOTAL	
J J	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 191 946	

(C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 42:

	GTT	rcgco	CTC .	AGAA	GGCT	GC C	TCGC	TGGT	C .CG	TTAA	CGGT	GGC	GCCA	CGT	CCGC	CCGTC	T 60
	CCG	CTT	CTG	CATC	GCGG	CT T	CGGC	GGCT	r cc	ACCT	AGAC	ACC	TAAC	AGT	CGCG	GAGCC	G 120
5	GCCC	CGT	CGT	GAGG	GGGT	CG G	CACG	GGGA	G TC	GGGC	GGTC	TTG	TGCA	TCT	TGGC	TACCT	G 180
	TGG	TCG/	AAG .	ATG	TCG	GAC	ATC	GGA (GAC	TGG	TTC .	AGG .	AGC .	ATC (CCG	GCG	229
			1	Met	Ser	Asp	Ile	Gly	Asp	Trp	Phe .	Arg	Ser	Ile	Pro .	Ala	
				1				5					10				
								GCC									277
ro	Ile	Thr	Arg	Tyr	Trp	Phe	Ala	Ala	Thr	Val	Ala	Val	Pro	Leu	Val	Gly	
		15					20					25					
								GCC									325
		Leu	Gly	Leu	Ile		Pro	Ala	Tyr	Leu	Phe	Leu	Trp	Pro	Glu	Ala	
	30					35					40					45	
L5								TGG									373
	Phe	Leu	Tyr	Arg			Ile	Trp	Arg			Thr	Ala	Thr		Tyr	
	即吓 C	CCT	000	CC 97	50		4.05			55		===			60		
								GGA									421
20	rne	FIG	Val	65 65		GIY	ini	Gly	70		Tyr	Leu	Val		Leu	Tyr	
	ттс	ТТА	ТАТ			ጥርጥ	ACC	CGA			A C A	GGA	CCT	75 ••••	CAT	ccc	469
								Arg									409
			80	01	,.	001		85	Deu	010	1111	GLY	90	THE	nsp	Gly	
	AGG	CCA		GAC	TAT	TTA	TTC	ATG	СТС	стс	: ጥጥጥ	AAC		АТТ	TGC	ATC	517
25								Met									
		95					100					105	•		,		
	GTG	ATT	ACT	GGC	TTA	GCA	ATG	GAT	ATG	CAG	TTG	CTG	ATG	ATT	CCT	CTG	565
								Asp									
	110					115					120					125	
30	ATC	ATG	TCA	GTA	CTT	TAT	GTC	TGG	GCC	CAG	CTG	AAC	AGA	GAC	ATG	ATT	613
	Ile	Met	Ser	Val	Leu	Tyr	Val	Trp	Ala	Gln	Leu	Asn	Arg	Asp	Met	Ile	
					130					135	,				140		
	GTA	TCA	TTT	TGG	TTT	GGA	ACA	CGA	TTT	' AAG	GCC	TGC	TAT	TTA	ccc	TGG	661
	Val	Ser	Phe	Trp	Phe	Gly	Thr	Arg	Phe	Lys	Ala	Cys	Tyr	Leu	Pro	Trp	
35				145	;				150)				155			
	GTT	ATC	CTT	GGA	TTC	AAC	TAT	ATC	ATC	GGA	GGC	TCG	GTA	ATC	AAT	GAG	709
	Val	Ile	Leu	Gly	Phe	Asn	Tyr	Ile	Ile	Gly	Gly	Ser	Va1	Ile	Asn	Glu	
			160					165					170				

	CTT	TTA	GGA	AAT	CTG	GTT	GGA	CAT	CTT	TAT	TTT	TTC	CTA	ATG	TTC	AGA	757
	Leu	Ile	Gly	Asn	Leu	Val	Gly	His	Leu	Tyr	Phe	Phe	Leu	Met	Phe	Arg	
		175					180					185					
	TAC	CCA	ATG	GAC	TTG	GGA	GGA	AGA	AAT	TTT	CTA	TCC	ACA	CCT	CAG	TTT	805
5	Tyr	Pro	Met	Asp	Leu	Gly	Gly	Arg	Asn	Phe	Leu	Ser	Thr	Pro	Gln	Phe	
	190					195					200					205	
•	TTG	TAC	CGC	TGG	CTG	CCC	AGT	AGG	AGA	GGA	GGA	GTA	TCA	GGA	TTT	GGT	853
	Leu	Tyr	Arg	Trp	Leu	Pro	Ser	Arg	Arg	Gly	Gly	Val	Ser	Gly	Phe	Gly	
					210					215					220		
10	GTG	CCC	CCT	GCT	AGC	ATG	AGG	CGA	GCT	GCT	GAT	CAG	AAT	GGC	GGA	GGC	901
	Val	Pro	Pro	Ala	Ser	Met	Arg	Arg	Ala	Ala	Asp	Gln	Asn	Gly	Gly	Gly	
				225					230					235			
	GGG	AGA	CAC	AAC	TGG	GGC	CAG	GGC	TTT	CGA	CTT	GGA	GAC	CAG	TGA	AGGG	950
	Gly	Arg	His	Asn	Trp	Gly	Gln	Gly	Phe	Arg	Leu	Gly	Asp	Gln			
15			240					245					250				
	GCGC	CCT	CGG (GCAG	CCGC	rc c	rctc/	AAGCC	ACA	ATTT	CTC	CCAC	STGC	rgg (GTGC	CTTAA	1010
	CAAC	CTGC	STT (CTGG(CTAAC	CA C	IGTT(GACC	TG	ACCCA	ACAC	TGA	ATGTA	AGT (CTTT	CAGTAC	1070
																SATTCT	1130
																CTGACT	1190
20	ACA?	rttt'	rtg (GTGT	CTTC	C T	rctc(CCCTI	TC	CGTC	rgaa	TAAT	rggg:	TTT :	TAGC	GGTCC	1250
																CTTATC	1310
																TAGAAG	1370
																TGCCAA	1430
																TAGCA	1490
25 .																TTCGAC	1550
																CACTG	1610
																STTTGT	1670
	,															AAATTT	1730
20																AGCTGG	1790
30																ATGCTC	1850
																TCATT	1910
																CCCCG	1970
																ragatc	2030
25																AATGGC	2090
35																CTGTG	2150
																CAGAGC	2210
																TTATT	2270
	TTA'	rgac(STT .	ATCT(GAAA(GC A	GACT	GTTAC	GAC	CAG	TTAT	GAGT	rggc	TGT (CACAC	CTTTGA	2330

133

	GGCAACTAAA	AAGGCTTCAA	ACGTTTTGAT	CAGTTTCTTT	TCAGGAAACA	TTGTGCTCTA	2390
	ACAGTATGAC	TATTCTTTCC	CCCACTCTTA	AACAGTGTGA	TGTGTGTTAT	CCTAGGAAAT	2450
	GAGAGTTGGC	AAACAACTTC	TCATTTTGAA	TAGAGTTTGT	GTGTACCTCT	CCATATTTAA	2510
	TTTATATGAT	AAAATAGGTG	GGGAGAGTCT	GAACCTTAAC	TGTCATGTTT	TGTTGTTCAT	2570
5	CTGTGGCCAC	AATAAAGTTT	ACTTGTAAAA	TTTTAGAGGC	CATTACTCCA	ATTATGTTGC	2630
	ACGTACACTC	ATTGTACAGG	CGTGGAGACT	CATTGTATGT	ATAAGAATAT	TCTGACAGTG	2690
	AGTGACCCGG	AGTCTCTGGT	GTACCCTCTT	ACCAGTCAGC	TGCCTGCGAG	CAGTCATTTT	2750
	TTCCTAAAGG	TTTACAAGTA	TTTAGAACTC	TTCAGTTCAG	GGCAAAATGT	TCATGAAGTT	2810
	ATTCCTCTTA	AACATGGTTA	GGAAGCTGAT	GACGTTATTG	ATTTTGTCTG	GATTATGTTT	2870
10	CTGGAATAAT	TTTACCAAAA	CAAGCTATTT	GAGTTTTGAC	TTGACAAGGC	AAAACATGAC	2930
	AGTGGATTCT	CTTTACAAAT	TGAAAAAAA	AATCCTTATT	TTGTATAAAG	GACTTCCCTT	2990
	TTTGTAAACT	AATCCTTTTT	ATTGGTAAAA	ATTGTAAATT	AAAATGTGCA	ACTTG	3045

- 15 (2) INFORMATION FOR SEQ ID NO: 43:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 653
 - (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
- 20 (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA
 - (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
- 25 (B) CELL KIND: Epidermoid carcinoma
 - (C) CELL LINE: KB
 - (D) CLONE NAME: HP10389
 - (ix) SEQUENCE CHARACTERISTICS:
- 30 (A) CHARACTERIZATION CODE: CDS

35

- (B) EXISTENCE POSITION: 63.. 383
- (C) CHARACTERIZATION METHOD: E
- (xi) SEQUENCE DESCRIPTION: SEQ ID NO: 43:

ATGACCTTCA CCGGGAGGCT GAGGTCGGAG TCCCGATTTT CTCCTGCTGC TGTGGCCCGG

AC ATG GCG ACT CCC GGC CCT GTG ATT CCG GAG GTC CCC TTT GAA CCA

Met Ala Thr Pro Gly Pro Val Ile Pro Glu Val Pro Phe Glu Pro

134

		1				5					10					15	
	TCG	AAG	CCT	CCA	GTC	ATT	GAG	GGG	CTG	AGC	CCC	ACT	GTT	TAC	AGG	AAT	155
	Ser	Lys	Pro	Pro	Val	Ile	Glu	Gly	Leu	Ser	Pro	Thr	Val	Tyr	Arg	Asn	
					20					25					30		
5	CCA	GAG	AGT	TTC	AAG	GAA	AAG	TTC	GTT	CGC	AAG	ACC	CGC	GAG	AAC	CCG	203
	Pro	Glu	Ser	Phe	Lys	Glu	Lys	Phe	Val	Arg	Lys	Thr	Arg	Glu	Asn	Pro	
				35					40					45			
	GTG	GTA	CCC	ATA	GGT	TGC	CTG	GCC	ACG	GCG	GCC	GCC	CTC	ACC	TAC	GGC	251
	Val	Val	Pro	Ile	Gly	Cys	Leu	Ala	Thr	Ala	Ala	Ala	Leu	Thr	Tyr	Gly	
10			50					55					60				
	CTC	TAC	TCC	TTC	CAC	CGG	GGC	AAC	AGC	CAG	CGC	TCT	CAG	CTC	ATG	ATG	299
	Leu	Tyr	Ser	Phe	His	Arg	Gly	Asn	Ser	Gln	Arg	Ser	Gln	Leu	Met	Met	•
		65					70					75					
									_						TTG		347
15	_	Thr	Arg	Ile	Ala		Gln	Gly	Phe	Thr		Ala	Ala	Ile	Leu		
	80					85					90					95	
												TAA	GCCC	AGG (GTCT(GGCCTT	400
	Gly	Leu	Ala	Val		Ala	Met	Lys	Ser	·							
20	C A A	A C C T	ccc	CACA	100	ATP TP.	CC	A A C C	C AC	105		CAC	TCCC	o com	٨٥٥٥	TGGGAC	460
20																TTTGTG	
																CATACT	
																CACTTG	
			TTC														653
25																	
	(2)	INF	ORMA	TION	FOR	SEQ	ID	NO:	44:								
				EQUE													
		,		(A)	LEN	GTH:	439										
30				(B)	TYP	E: N	ucle	ic a	cid								
				(C)	STR	ANDE	DNES	S: D	oubl	e							
				(D)	TOP	OLOG	Y: L	inea	r								
		(ii)	SEQU	ENCE	KIN	D: c	DNA	to m	RNA							
35		((vi)	ORIG	INAL	, sou	RCE:										

(A) ORGANISM: Homo sapiens (B) CELL KIND: Stomach cancer (D) CLONE NAME: HP10408

135

(ix) SEQUENCE CHARACTERISTICS:

	(A) CHARACTERIZATION CODE: CDS											
	(B) EXISTENCE POSITION: 75 311											
	(C) CHARACTERIZATION METHOD: E											
5												
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 44:											
	GTAGAAACAG GCCTGTTAAG GAGAGGCCAC CGGGACTTCA GTGTCTCCTC CATCCCAGGA	60										
	GCGCAGTGGC CACT ATG GGG TCT GGG CTG CCC CTT GTC CTC TTG ACC	110										
10	Met Gly Ser Gly Leu Pro Leu Val Leu Leu Thr											
	1 5 10											
	CTC CTT GGC AGC TCA CAT GGA ACA GGG CCG GGT ATG ACT TTG CAA CTG	158										
	Leu Leu Gly Ser Ser His Gly Thr Gly Pro Gly Met Thr Leu Gln Leu											
	15 20 25											
15	AAG CTG AAG GAG TCT TTT CTG ACA AAT TCC TCC TAT GAG TCC AGC TTC	206										
	Lys Leu Lys Glu Ser Phe Leu Thr Asn Ser Ser Tyr Glu Ser Ser Phe											
	30 35 40											
	CTG GAA TTG CTT GAA AAG CTC TGC CTC CTC CTC CAT CTC CCT TCA GGG	254										
	Leu Glu Leu Leu Glu Lys Leu Cys Leu Leu Leu His Leu Pro Ser Gly											
20	45 50 55 60											
	ACC AGC GTC ACC CTC CAC CAT GCA AGA TCT CAA CAC CAT GTT GTC TGC	302										
	Thr Ser Val Thr Leu His His Ala Arg Ser Gln His His Val Val Cys											
	65 70 75											
	AAC ACA TGACAGCCAT TGAAGCCTGT GTCCTTCTTG GCCCGGGCTT TTGGGCCGGG GA	360										
25	Asn Thr											
	TGCAGGAGGC AGGCCCCGAC CCTGTCTTTC AGCAGGCCCC CACCCTCCTG AGTGGCAATA	420										
	AATAAAATTC GGTATGCTG	439										
30												
	(2) INFORMATION FOR SEQ ID NO: 45:											
	(i) SEQUENCE CHARACTERISTICS:											
	(A) LENGTH: 1131											
	(B) TYPE: Nucleic acid											
35	(C) STRANDEDNESS: Double											
	(D) TOPOLOGY: Linear											
	(ii) SEQUENCE KIND: cDNA to mRNA											

	(vi) ORIGINAL SOURCE: (A) ORGANISM: Homo sapiens																
				(A)	ORGA	MISH	i: Ho	omo s	sapie	ens							
				(B)	CELI	. KIN	ID: S	Stome	ich c	ance	r						
				(D)	CLO	IE NA	ME:	HP10	412								
5																	
		(i	x) S	EQUE	ENCE	CHAF	ACTI	ERIST	CICS:	:				•			
	(A) CHARACTERIZATION CODE: CDS																
	(B) EXISTENCE POSITION: 56 1000 (C) CHARACTERIZATION METHOD: E																
	(C) CHARACTERIZATION METHOD: E																
10	(wi) CEANENCE DECORTORION, ORG. TO NO. (5																
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 45:																
	CTATGAGATC CCGGCCTCAG GGTCGACGCA GTCGTTCTGC ACTGAGGCCC TCGTC ATG														F.0		
	CTATGAGATC CCGGCCTCAG GGTGGACGCA GTGGTTCTGC ACTGAGGCCC TCGTC ATG Met														58		
15	net 1																
	GTG (GCG	CCT	GTG	TGG	TAC	TTG	GTA	GCG	GCG	GCT	CTG	СТА	GTC	GGC		106
	Val A																
				5	•	•			10					15	·		
	ATC (CTC	TTC	CTG	ACT	CGC	AGC	CGG	GGC	CGG	GCG	GCA	TCA	GCC	GGC	CAA	154
20	Ile !	Leu	Phe	Leu	Thr	Arg	Ser	Arg	Gly	Arg	Ala	Ala	Ser	Ala	Gly	Gln	
			20					25					30				
	GAG (CCA	CTG	CAC	AAT	GAG	GAG	CTG	GCA	GGA	GCA	GGC	CGG	GTG	GCC	CAG	202
	Glu	Pro	Leu	His	Asn	Glu	Glu	Leu	Ala	Gly	Ala	Gly	Arg	Val	Ala	Gln	
		35					40					45					
25	CCT																250
	Pro	Gly	Pro	Leu	Glu		Glu	Glu	Pro	Arg		Gly	Gly	Arg	Pro		
	50	000	400	040	omo.	55		000	0.004	0.0	60		000	004	000	65	200
	CGC																298
30	Arg .	vrg	vrg	vsh	70	GIY	261	wrg	ren	75	WIR	GIII	ALE	KLR	80	GIII	
30	CGG	GTG	GCC	TGG		GAA	GCA	GAT	GAG		GAG	GAG	GAA	GCT		ATC	346
	Arg																
	J			85				•	90					95			
	CTA	GCC	CAG	GAG	GAG	GAA	GGT	GTC	GAG	AAG	CCA	GCG	GAA	ACT	CAC	CTG	394
35	Leu .	Ala	Gln	Glu	Glu	Glu	Gly	Val	Glu	Lys	Pro	Ala	Glu	Thr	His	Leu	
			100					105					110				
	TCG	GGG	AAA	ATT	GGA	GCT	AAG	AAA	CTG	CGG	AAG	CTG	GAG	GAG	AAA	CAA	442
	Ser	Gly	Lys	Ile	Gly	Ala	Lys	Lys	Leu	Arg	Lys	Leu	Glu	Glu	Lys	Gln	

		112					120					125					
	GCG	CGA	AAG	GCC	CAG	CGT	GAG	GCA	GAG	GAG	GCT	GAA	CGT	GAG	GAG	CGG	490
	Ala	Arg	Lys	Ala	Gln	Arg	Glu	Ala	Glu	Glu	Ala	Glu	Arg	Glu	Glu	Arg	
	130					135					140					145	
5	AAA	CGA	CTC	GAG	TCC	CAG	CGC	GAA	GCT	GAG	TGG	AAG	AAG	GAG	GAG	GAG	538
	Lys	Arg	Leu	Glu	Ser	Gln	Arg	Glu	Ala	Glu	Trp	Lys	Lys	Glu	Glu	Glu	
					150					155					160		
	CGG	CTT	CGC	CTG	GAG	GAG	GAG	CAG	AAG	GAG	GAG	GAG	GAG	AGG	AAG	GCC	586
	Arg	Leu	Arg	Leu	Glu	Glu	Glu	Gln	Lys	Glu	Glu	Glu	Glu	Arg	Lys	Ala	
10				165					170					175			
	CGC	GAG	GAG	CAG	GCC	CAG	CGG	GAG	CAT	GAG	GAG	TAC	CTG	AAA	CTG	AAG	634
	Arg	Glu	Glu	Gln	Ala	G1n	Arg	Glu	His	Glu	Glu	Tyr	Leu	Lys	Leu	Lys	
			180					185					190				
	GAG	GCC	TTT	GTG	GTG	GAG	GAG	GAA	GGC	GTA	GGA	GAG	ACC	ATG	ACT	GAG	682
15	Glu	Ala	Phe	Val	Val	Glu	Glu	Glu	Gly	Val	Gly	Glu	Thr	Met	Thr	Glu	
		195					200					205					
	GAA	CAG	TCC	CAG	AGC	TTC	CTG	ACA	GAG	TTC	ATC	AAC	TAC	ATC	AAG	CAG	730
	Glu	Gln	Ser	Gln	Ser	Phe	Leu	Thr	Glu	Phe	Ile	Asn	Tyr	Ile	Lys	Gln	
	210					215					220					225	
20	TCC	AAG	GTT	GTG	CTC	TTG	GAA	GAC	CTG	GCT	TCC	CAG	GTG	GGC	CTA	CGC	778
	Ser	Lys	Val	Val	Leu	Leu	Glu	Asp	Leu	Ala	Ser	Gln	Val	Gly	Leu	Arg	
					230					235					240		
	ACT	CAG	GAC	ACC	ATA	AAT	CGC	ATC	CAG	GAC	CTG	CTG	GCT	GAG	GGG	ACT	826
	Thr	Gln	Asp	Thr	Ile	Asn	Arg	Ile	Gln	Asp	Leu	Leu	Ala	Glu	Gly	Thr	
25				245					250					255			
	ATA	ACA	GGT	GTG	ATT	GAC	GAC	CGG	GGC	AAG	TTC	ATC	TAC	ATA	ACC	CCA	874
	Ile	Thr	Gly	Val	Ile	Asp	Asp	Arg	Gly	Lys	Phe	Ile	Tyr	Ile	Thr	Pro	
			260					265					270				
	GAG	GAA	CTG	GCC	GCC	GTG	GCC	AAC	TTC	ATC	CGA	CAG	CGG	GGC	CGG	GTG	922
30	Glu	Glu	Leu	Ala	Ala	Val	Ala	Asn	Phe	Ile	Arg	Gln	Arg	Gly	Arg	Val	
		275					280					285					
	TCC	ATC	GCC	GAG	CTT	GCC	CAA	GCC	AGC	AAC	TCC	CTC	ATC	GCC	TGG	GGC	970
	Ser	Ile	Ala	Glu	Leu	Ala	Gln	Ala	Ser	Asn	Ser	Leu	Ile	Ala	Trp	Gly	
	290					295					300					305	
35	CGG	GAG	TCC	CCT	GCC	CAA	GCC	CCA	GCC	TGAC	CCCC	AGT (CTTC	CCTC	T TO	G	1020
	Arg	Glu	Ser	Pro	Ala	Gln	Ala	Pro	Ala								
					310												
	ACTO	CAGA	GTT (GTGT	rggc	CT AC	CTG	CTA	r ACA	ATCT	CAT	CCC	ccc	CAC	CATCO	TGGGG	1080

138

1131

303

AAGTGATGGT GTGGCCAGGC AGTTATAGAT TAAAGGCCTG TGAGTACTGC T

	(2) INFORMATION	FOR SEQ ID	NO: 46:				
5	(i) SEQUE	NCE CHARACTE	RISTICS:				
	(A)	LENGTH: 187	5				
	(B)	TYPE: Nucle	ic acid				
	(C)	STRANDEDNES	S: Double	e			
	(D)	TOPOLOGY: L	inear				
10	(ii) SEQU	ENCE KIND: c	DNA to m	RNA			
	(vi) ORIG	INAL SOURCE:				•	
	(A)	ORGANISM: H	omo sapi	ens			
		CELL KIND:	•				
15	(D)	CLONE NAME:	HP10413				
	(in) SEON	ENOD CUADACE					
		ENCE CHARACT					
		CHARACTERIZ. EXISTENCE P					
20	•	CHARACTERIZ.			D		
	(0)	CIMICACTER 12.	ALLON FIE.	Inop: E			
	(xi) SEQU	ENCE DESCRIP	TION: SEC	Q ID NO:	46:		
	CTCGCTCGCT CAGA	GGGAGG AGAAA	GTGGC GAG	GTTCCGGA	TCCCTGC	CTA GCGCGGCCCA	60
25	ACCTTTACTC CAGA	GATC ATG GCT	GCC GAG	GAT GTG	GTG GCG	ACT GGC GCC	111
		Met Ala	Ala Glu	Asp Val	Val Ala	Thr Gly Ala	
		1		5		10	
	GAC CCA AGC GAT	CTG GAG AGC	GGC GGG	CTG CTG	CAT GAG	ATT TTC ACG	159
	Asp Pro Ser Asp	Leu Glu Ser	Gly Gly	Leu Leu	His Glu	Ile Phe Thr	
30	. 15		20			25	
	TCG CCG CTC AAC	CTG CTG CTG	CTT GGC	CTC TGC	ATC TTC	CTG CTC TAC	207
	Ser Pro Leu Asn	Leu Leu Leu	Leu Gly	Leu Cys	Ile Phe	Leu Leu Tyr	
	30		35		40		
	AAG ATC GTG CGC						255
35	Lys Ile Val Arg	Gly Asp Gln	Pro Ala	Ala Ser	Gly Asp	Ser Asp Asp	
	45	50			55		

GAC GAG CCG CCC CCT CTG CCC CGC CTC AAG CGG CGC GAC TTC ACC CCC

Asp Glu Pro Pro Pro Leu Pro Arg Leu Lys Arg Arg Asp Phe Thr Pro

	60					65					70					75	
	GCC	GAG	CTG	CGG	CGC	TTC	GAC	GGC	GTC	CAG	GAC	CCG	CGC	ATA	CTC	ATG	351
	Ala	Glu	Leu	Arg	Arg	Phe	Asp	Gly	Val	G1n	Asp	Pro	Arg	Ile	Leu	Met	
					80					85					90		
5	GCC	ATC	AAC	GGC	AAG	GTG	TTC	GAT	GTG	ACC	AAA	GGC	CGC	AAA	TTC	TAC	399
	Ala	Ile	Asn	Gly	Lys	Val	Phe	Asp	Val	Thr	Lys	Gly	Arg	Lys	Phe	Tyr	
				95					100					105			
	GGG	CCC	GAG	GGG	CCG	TAT	GGG	GTC	TTT	GCT	GGA	AGA	GAT	GCA	TCC	AGG	447
	Gly	Pro	Glu	Gly	Pro	Tyr	Gly	Val	Phe	Ala	Gl y	Arg	Asp	Ala	Ser	Arg	
10			110					115					120				
	GGC	CTT	GCC	ACA	TTT	TGC	CTG	GAT	AAG	GAA	GCA	CTG	AAG	GAT	GAG	TAC	495
	Gly	Leu	Ala	Thr	Phe	Cys	Leu	Asp	Lys	Glu	Ala	Leu	Lys	Asp	Glu	Tyr	
		125					130					135					
	GAT	GAC	CTT	TCT	GAC	CTC	ACT	GCT	GCC	CAG	CAG	GAG	ACT	CTG	AGT	GAC	543
15	Asp	Asp	Leu	Ser	Asp	Leu	Thr	Ala	Ala	Gln	Gln	Glu	Thr	Leu	Ser	Asp	
	140					145					150					155	
	TGG	GAG	TCT	CAG	TTC	ACT	TTC	AAG	TAT	CAT	CAC	GTG	GGC	AAA	CTG	CTG	591
	Trp	G1u	Ser	Gln	Phe	Thr	Phe	Lys	Tyr	His	His	Val	Gly	Lys	Leu	Leu	
					160					165					170		
20	AAG	GAG	GGG	GAG	GAG	CCC	ACT	GTG	TAC	TCA	GAT	GAG	GAA	GAA	CCA	AAA	639
	Lys	Glu	Gly	Glu	Glu	Pro	Thr	Val	Tyr	Ser	Asp	Glu	Glu	Glu	Pro	Lys	
				175					180					185			
	GAT	GAG	AGT	GCC	CGG	AAA	AAT	GAT	TAA	AGCA:	PTC A	AGTG(GAAG'	ra t	ATCT	AT	690
	Asp	Glu	Ser	Ala	Arg	Lys	Asn	Asp									
25			190					195									
	TTT:	rgta'	TTT	TGCA	AAAT	CA T	TTGT.	AACA	G TC	CACT	CTGT	CTT	AAAT	ACA '	TAGT	GATTAC	750
	AAT	ATTT	AGA .	AAGT'	TTTG	AG C	ACTT	GCTA'	AA T	GTTT:	TTTA	TAA	CATC	ACT .	AGTG	ACACTA	810
	ATA	TAAA	TAA	CTTC'	TTAG	AA T	GCAT	GATG'	r GT	rtgt(GTGT	CAC	AAAT	CCA	GAAA	GTGAAC	870
	TGC	AGTG	CTG	TAAT	ACAC	AT G	TTAA	TACT	G TT	rttc:	rtct	ATC	TGTA	GTT .	AGTA	CAGGAT	- 930
30	GAA'	TTTA	TAA	GTGT'	TTTT	CC T	GAGA	GACA	A GG	AAGA	CTTG	GGT	ATTT	ccc .	AAAA	CAGGTA	990
	AAA	ATCT	TAA .	ATGT	GCAC	CA A	GAGC	AAAG	G AT	CAAC'	TTTT	AGT	CATG	ATG	TTCT	GTAAAG	1050
	ACA	ACAA	ATC	CCTT	TTTT'	TT T	CTCA	ATTG	A CT	TAAC'	TGCA	TGA	TTTC	TGT	TTTA'	TCTACC	1110
	TCT	AAAG	CAA	ATCT	GCAG'	TG T	TCCA	AAGA	C TT	TGGT	ATGG	ATT	AAGC	GCT (GTCC	AGTAAC	1170
	AAA	ATGA	AAT	CTCA	AAAC.	AG A	GCTC.	AGCT	G CA	AAAA	AGCA	TAT	TTTC	TGT (GTTT(CTGGAC	1230
35	TGC	ACTG	TTG	TCCT	TGCC	CT C	ACAT.	AGAC.	A CT	CAGA	CACC	CTC	ACAA	ACA	CAGT	AGTCTA	1290
	TAG	TTAG	GAT	TAAA	ATAG	GA T	CTGA	ACAT	T CA	AAAG.	AAAG	CTT	TGGA	AAA .	AAAG	AGCTGG	1350
	CTG	GCCT	AAA	AACC	TAAA	TA T	ATGA	TGAA	G AT	TGTA	GGAC	TGT	CTTC	CCA .	AGCC	CCATGT	-1410
	TCA	TGGT	GGG	GCAA	TGGT	TA T	TTGG	TAT	T TT.	ACTC.	TTAA	GGT	TACT	CTC .	ATTT(GAAATG	1470

	AGGGAGGGAC ATACAGAATA GGAACAGGTG TTTGCTCTCC TAAGAGCCTT CATGCACACC	1530
	CCTGAACCAC GAGGAAACAG TACAGTCGCT AGTCAAGTGG TTTTTAAAGT AAAGTATATT	1590
	CATAAGGTAA CAGTTATTCT GTTGTTATAA AACTATACCC ACTGCAAAAG TAGTAGTCAA	1650
	GTGTCTAGGT CTTTGATATT GCTCTTTTGG TTAACACTAA GCTTAAGTAG ACTATACAGT	1710
5	TGTATGAATT TGTAAAAGTA TATGAACACC TAGTGAGATT TCAAACTTGT AATTGTGGTT	1770
	AAATAGTCAT TGTATTTTCT TGTGAACTGT GTTTTATGAT TTTACCTCAA ATCAGAAAAC	1830
	AAAATGATGT GCTTTGGTCA GTTAATAAAA ATGGTTTTAC CCACT	1875
10	(2) INFORMATION FOR SEQ ID NO: 47:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 1563	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
15	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
20	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10415	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
25	(B) EXISTENCE POSITION: 72 1460	
	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 47:	
2.0		
30	AAATTGGGCC AGGCTGAGGC GCTGCTGCTG GAGCGGCCGA TCCGAGACGT GGCTCCCTGG	60
	GCGGCAGAAC C ATG TTG GAC TTC GCG ATC TTC GCC GTT ACC TTC TTG CTG	110
	Met Leu Asp Phe Ala Ile Phe Ala Val Thr Phe Leu Leu 1 5 10	
	GCG TTG GTG GGA GCC GTG CTC TAC CTC TAT CCG GCT TCC AGA CAA GCT	158
35	Ala Leu Val Gly Ala Val Leu Tyr Leu Tyr Pro Ala Ser Arg Gln Ala	130
J.	15 . 20 . 25	
	GCA GGA ATT CCA GGG ATT ACT CCA ACT GAA GAA AAA GAT GGT AAT CTT	206
	Ala Gly Ile Pro Gly Ile Thr Pro Thr Glu Glu Lys Asp Gly Asn Leu	
	•	

	30					35					40					45	
	CCA	GAT	ATT	GTG	AAT	AGT	GGA	AGT	TTG	CAT	GAG	TTC	CTG	GTT	AAT	TTG	254
	Pro	Asp	Ile	Val	Asn	Ser	Gly	Ser	Leu	His	Glu	Phe	Leu	Val	Asn	Leu	
					50					55					60		
5	CAT	GAG	AGA	TAT	GGG	CCT	GTG	GTC	TCC	TTC	TGG	TTT	GGC	AGG	CGC	CTC	302
	His	Glu	Arg	Tyr	Gly	Pro	Val	Val	Ser	Phe	Trp	Phe	Gly	Arg	Arg	Leu	
				65					70					75			
	GTG	GTT	AGT	TTG	GGC	ACT	GTT	GAT	GTA	CTG	AAG	CAG	CAT	ATC	AAT	CCC	350
	Val	Val	Ser	Leu	Gly	Thr	Val	Asp	Val	Leu	Lys	Gln	His	Ile	Asn	Pro	
10			80					85					90				
	AAT	AAG	ACA	TTG	GAC	CCT	TTT	GAA	ACC	ATG	CTG	AAG	TCA	TTA	TTA	AGG	398
•	Asn	Lys	Thr	Leu	Asp	Pro	Phe	Glu	Thr	Met	Leu	Lys	Ser	Leu	Leu	Arg	•
		95					100					105					
	TAT	CAA	TCT	GGT	GGT	GGC	AGT	GTG	AGT	GAA	AAC	CAC	ATG	AGG	AAA	AAA	446
15	Tyr	Gln	Ser	Gly	Gly	Gly	Ser	Val	Ser	Glu	Asn	His	Met	Arg	Lys	Lys	
	110					115					120					125	
	TTG	TAT	GAA	AAT	GGT	GTG	ACT	GAT	TCT	CTG	AAG	AGT	AAC	TTT	GCC	CTC	494
	Leu	Tyr	Glu	Asn	Gly	Val	Thr	Asp	Ser	Leu	Lys	Ser	Asn	Phe	Ala	Leu	
					130					135					140		
20				CTT													542
	Leu	Leu	Lys	Leu	Ser	Glu	Glu	Leu		Asp	Lys	Trp	Leu		Tyr	Pro	
				145					150					155			
	•			CAC													590
25	GIu	Thr		His	Val	Pro	Leu		Gln	His	Met	Leu	_	Phe	Ala	Met	
25	440	808	160	404			054	165					170		0 t m	010	
				ACA													638
	гÄг			Thr	Gin	met		met	GIÀ	Ser	Thr		GIU	Asp	Asp	GIN	
	CAA	175		CGC	mm/c	040	180	A A 470	C 4 m	000	404	185	moo.	m c m	CAC	A TOTO	606
30				Arg													686
30	190		116	vrR	rne	195	ьуз	Vell	nrs	GIY	200	val	пр	SET	GIU	205	
			GGC	TTT	СТА		ccc	ጥ ር ል	ር ጥጥ	САТ		4 A C	ልጥር	ልሮሞ	ccc		734
				Phe													734
	01)	2,0	02)		210	_	01)	DCI	БСЦ	215	Буз	nsn	1100	1111	220	Цуб	
35	AAA	CAA	TAT	GAA			CTC	A TC	CAA		GAG	ፐርሞ	ርጥጥ	ΤΤΔ		AAC	782
				Glu													702
	-,5		-,-	225			J-04		230		Jiu	JUL		235		# -	
	ATC	АТА	AAA	GAA		AAA	GGA	AGG			AGT	CAA	САТ			ATT	830

	Ile	Ile	Lys	Glu	Arg	Lys	Gly	Arg	Asn	Phe	Ser	Gln	His	Ile	Phe	Ile	
			240					245					250				
	GAC	TCC	TTA	GTA	CAA	GGG	AAC	CTT	AAT	GAC	CAA	CAG	ATC	CTA	GAA	GAC	878
	Asp	Ser	Leu	Val	Gln	Gly	Asn	Leu	Asn	Asp	Gln	Gln	Ile	Leu	Glu	Asp	
5		255					260					265					
	AGT	ATG	ATA	TTT	TCT	CTG	GCC	AGT	TGC	ATA	ATA	ACT	GCA	AAA	TTG	TGT	926
	Ser	Met	Ile	Phe	Ser	Leu	Ala	Ser	Cys	Ile	Ile	Thr	Ala	Lys	Leu	Cys	
	270					275					280					285	
	ACC	TGG	GCA	ATC	TGT	TTT	TTA	ACC	ACC	TCT	GAA	GAA	GTT	CAA	AAA	AAA	974
10	Thr	Trp	Ala	Ile	Cys	Phe	Leu	Thr	Thr	Ser	Glu	Glu	Val	Gln	Lys	Lys	
					290					295					300		
•	TTA	TAT	GAA	GAG	ATA	AAC	CAA	GTT	TTT	GGA	AAT	GGT	CCT	GTT	ACT	CCA	1022
	Leu	Tyr	Glu	Glu	Ile	Asn	Gln	Val	Phe	Gly	Asn	Gly	Pro	Val	Thr	Pro	
				305					310					315			
15	GAG	AAA	ATT	GAG	CAG	CTC	AGA	TAT	TGT	CAG	CAT	GTG	CTT	TGT	GAA	ACT	1070
	G1u	Lys	Ile	Glu	Gln	Leu	Arg	Tyr	Cys	Gln	His	Val	Leu	Cys	Glu	Thr	
			320					325					330				
	GTT	CGA	ACT	GCC	AAA	CTG	ACT	CCA	GTT	TCT	GCC	CAG	CTT	CAA	GAT	ATT	1118
	Val	Arg	Thr	Ala	Lys	Leu	Thr	Pro	Val	Ser	Ala	Gln	Leu	Gln	Asp	Ile	
20		335					340					345					
	GAA	GGA	AAA	ATT	GAC	CGA	TTT	ATT	ATT	CCT	AGA	GAG	ACC	CTC	GTC	CTT	1166
	Glu	Gly	Lys	Ile	Asp	Arg	Phe	Ile	Ile	Pro	Arg	Glu	Thr	Leu	Val	Leu	
	350					355					360					365	
	TAT	GCC	CTT	GGT	GTG	GTA	CTT	CAG	GAT	CCT	AAT	ACT	TGG	CCA	TCT	CCA	1214
25	Tyr	Ala	Leu	Gly	Val	Val	Leu	Gln	Asp	Pro	Asn	Thr	Trp	Pro	Ser	Pro	
					370					375					380		
	CAC	AAG	TTT	GAT	CCA	GAT	CGG	TTT	GAT	GAT	GAA	TTA	GTA	ATG	AAA	ACT	1262
	His	Lys	Phe	Asp	Pro	Asp	Arg	Phe	Asp	Asp	Glu	Leu	Val	Met	Lys	Thr	
				385					390					395			
30	TTT	TCC	TCA	CTT	GGA	TTC	TCA	GGC	ACA	CAG	GAG	TGT	CCA	GAG	TTG	AGG	1310
	Phe	Ser	Ser	Leu	Gly	Phe	Ser	Gly	Thr	Gln	Glu	Cys	Pro	Glu	Leu	Arg	
			400					405					410				
	TTT	GCA	TAT	ATG	GTG	ACC	ACA	GTA	CTT	CTT	AGT	GTA	TTG	GTG	AAG	AGA	1358
	Phe	Ala	Tyr	Met	Val	Thr	Thr	Val	Leu	Leu	Ser	Val	Leu	Val	Lys	Arg	
35		415					420					425					
	CTG	CAC	CTA	CTT	TCT	GTG	GAG	GGA	CAG	GTT	ATT	GAA	ACA	AAG	TAT	GAA	1406
	Leu	His	Leu	Leu	Ser	Val	Glu	Gly	Gln	Val	Ile	Glu	Thr	Lys	Tyr	Glu	
	430					435					440					445	

	CTG GTA ACA TCA TCA AGG GAA GAA GCT TGG ATC ACT GTC TCA AAG AGA	1454
	Leu Val Thr Ser Ser Arg Glu Glu Ala Trp Ile Thr Val Ser Lys Arg	
	450 455 460	
	TAT TAAAATTTTA TACATTTAAA ATCATTGTTA AATTGATTGA GGAAAACAAC CAT	1510
5	Tyr	
	TTAAAAAAA TCTATGTTGA ATCCTTTTAT AAACCAGTAT CACTTTGTAA TAT	1563
10	(2) INFORMATION FOR SEQ ID NO: 48:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 2030	
	(B) TYPE: Nucleic acid	
15	(C) STRANDEDNESS: Double	
13	(D) TOPOLOGY: Linear (ii) SEQUENCE KIND: cDNA to mRNA	
	(II) SEQUENCE KIND: COMA CO MKNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
20	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10419	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
25	(B) EXISTENCE POSITION: 171 914	
	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 48:	
20	CAMMUS COOK THE COOK TO SEE TH	
30	CATTTGGGGT TTCGGTTCCC CCCCTTCCCC TTCCCCGGGG TCTGGGGGTG ACATTGCACC	60
	GCGCCCCTCG TGGGGTCGCG TTGCCACCCC ACGCGGACTC CCCAGCTGGC GCGCCCCTCC	120
	CATTTGCCTG TCCTGGTCAG GCCCCCACCC CCCTTCCCAC CTGACCAGCC ATG GGG	176
	Met Gly	
35	GCT GCG GTG TTT TTC GGC TGC ACT TTC GTC GCG TTC GGC CCG GCC TTC	221
J.J	Ala Ala Val Phe Phe Gly Cys Thr Phe Val Ala Phe Gly Pro Ala Phe	224
	5 10 15	
	GCG CTT TTC TTG ATC ACT GTG GCT GGG GAC CCG CTT CGC GTT ATC ATC	272
	and the state of t	412

	Ala	Leu	Phe	Leu	Ile	Thr	Val	Ala	Gly	Asp	Pro	Leu	Arg	Val	Ile	Ile	
		20					25					30					
	CTG	GTC	GCA	GGG	GCA	TTT	TTC	TGG	CTG	GTC	TCC	CTG	CTC	CTG	GCC	TCT	320
	Leu	Val	Ala	G1y	Ala	Phe	Phe	Trp	Leu	Val	Ser	Leu	Leu	Leu	Ala	Ser	
5	35					40					45					50	
	GTG	GTC	TGG	TTC	ATC	TTG	GTC	CAT	GTG	ACC	GAC	CGG	TCA	GAT	GCC	CGG	368
	Val	Val	Trp	Phe	Ile	Leu	Val	His	Val	Thr	Asp	Arg	Ser	Asp	Ala	Arg	
					55					60					65		
	CTC	CAG	TAC	GGC	CTC	CTG	ATT	TTT	GGT	GCT	GCT	GTC	TCT	GTC	CTT	CTA	416
10	Leu	Gln	Tyr	Gly	Leu	Leu	Ile	Phe	Gly	Ala	Ala	Val	Ser	Val	Leu	Leu	
				70					75					80			
	CAG	GAG	GTG	TTC	CGC	TTT	GCC	TAC	TAC	AAG	CTG	CTT	AAG	AAG	GCA	GAT	464
	Gln	Glu	Val	Phe	Arg	Phe	Ala	Tyr	Tyr	Lys	Leu	Leu	Lys	Lys	Ala	Asp	
			85					90					95				
L5	GAG	GGG	TTA	GCA	TCG	CTG	AGT	GAG	GAC	GGA	AGA	TCA	CCC	ATC	TCC	ATC	512
	Glu	Gly	Leu	Ala	Ser	Leu	Ser	Glu	Asp	Gly	Arg	Ser	Pro	Ile	Ser	Ile	
		100					105					110					
	CGC	CAG	ATG	GCC	TAT	GTT	TCT	GGT	CTC	TCC	TTC	GGT	ATC	ATC	AGT	GGT	560
	Arg	Gln	Met	Ala	Tyr	Val	Ser	Gly	Leu	Ser	Phe	Gly	Ile	Ile	Ser	Gly	
20	115					120					125					130	
	GTC	TTC	TCT	GTT	ATC	AAT	ATT	TTG	GCT	GAT	GCA	CTT	GGG	CCA	GGT	GTG	608
	Val	Phe	Ser	Val	Ile	Asn	Ile	Leu	Ala	Asp	Ala	Leu	Gly	Pro	Gly	Val	
					135					140					145		
	•							CCC									656
25	Val	Gly	Ile	His	Gly	Asp	Ser	Pro	Tyr	Tyr	Phe	Leu	Thr	Ser	Ala	Phe	
				150					155					160			
	CTG	ACA	GCA	GCC	ATT	ATC	CTG	CTC	CAT	ACC	TTT	TGG	GGA	GTT	GTG	TTC	704
	Leu	Thr	Ala	Ala	Ile	Ile	Leu	Leu	His	Thr	Phe	Trp	Gly	Val	Val	Phe	
			165					170					175		٠		
30	TTT	GAT	GCC	TGT	GAG	AGG	AGA	CGG	TAC	TGG	GCT	TTG	GGC	CTG	GTG	GTT	752
	Phe	Asp	Ala	Cys	Glu	Arg	Arg	Arg	Tyr	Trp	Ala	Leu	Gly	Leu	Val	Val	
		180					185					190					
								GGA									800
	G1y	Ser	His	Leu	Leu	Thr	Ser	Gly	Leu	Thr	Phe	Leu	Asn	Pro	Trp	Tyr	
35	195					200					205					210	
								TAT									848
	Glu	Ala	Ser	Leu	Leu	Pro	Ile	Tyr	Ala	Val	Thr	Val	Ser	Met	Gly	Leu	
					215					220					225		

145

	TGG GCC T	TC ATC ACA	GCT GGA GGG	TCC CTC CGA	AGT ATT CAG CGC	AGC 896
	Trp Ala Pl	he Ile Thr	Ala Gly Gly	Ser Leu Arg	Ser Ile Gln Arg	Ser
		230		235	240	
	CTC TTG TO	GT AAG GAC	TGACTACCTG	GACTGATCGC C	TGACAGATC CCACCTG	CC 950
5	Leu Leu Cy	ys Lys Asp				
	24	45				
	TGTCCACTG	C CCATGACTG	A GCCCAGCCC	C AGCCCGGGTC	CATTGCCCAC ATTCT	CTGTC 1010
	TCCTTCTCG:	T CGGTCTACC	C CACTACCTC	C AGGGTTTTGC	TTTGTCCTTT TGTGA	ACCGTT 1070
	AGTCTCTAAG	G CTTTACCAG	G AGCAGCCTG	G GTTCAGCCAG	TCAGTGACTG GTGGG	STTTGA 1130
10	ATCTGCACT:	T ATCCCCACC	A CCTGGGGAC	с сссттеттет	GTCCAGGACT CCCCC	TGTGT 1190
	CAGTGCTCT	G CTCTCACCC	T GCCCAAGAC	T CACCTCCCTT	CCCCTCTGCA GGCCG	ACGGC 1250
	AGGAGGACA	G TCGGGTGAT	G GTGTATTCT	G CCCTGCGCAT	CCCACCCGAG GACTG	GAGGGA 1310
	ACCTAGGGG	G GACCCCTGG	G CCTGGGGTG	C CCTCCTGATG	TCCTCGCCCT GTATT	TTCTCC 1370
	ATCTCCAGT	T CTGGACAGT	G CAGGTTGCC	A AGAAAAGGGA	CCTAGTTTAG CCATT	GCCCT 1430
15	GGAGATGAA	A TTAATGGAG	G CTCAAGGAT	A GATGAGCTCT	GAGTTTCTCA GTACT	CCCTC 1490
	AAGACTGGA	C ATCTTGGTC	T TTTTCTCAG	G CCTGAGGGG	AACCATTTT GGTGT	TGATAA 1550
	ATACCCTAA	A CTGCCTTTT	т ттсттттт	G AGGTGGGGG	AGGGAGGAGG TATA	TTGGAA 1610
	CTCTTCTAA	C CTCCTTGGG	C TATATTTTC	T CTCCTCGAGT	TGCTCCTCAT GGCTG	GGCTC 1670
	ATTTCGGTC	с стттстсст	T GGTCCCAGA	C CTTGGGGGAA	AGGAAGGAAG TGCAT	rgtttg 1730
20	GGAACTGGC	A TTACTGGAA	C TAATGGTTT	T AACCTCCTTA	ACCACCAGCA TCCCT	TCCTCT 1790
	CCCCAAGGT	G AAGTGGAGG	G TGCTGTGGT	G AGCTGGCCAC	TCCAGAGCTG CAGTO	GCCACT 1850
	GGAGGAGTC	A GACTACCAT	G ACATCGTAG	G GAAGGAGGG	AGATTTTTT GTAG	TTTTA 1910
·	ATTGGGGTG	T GGGAGGGG	G GGGAGGTTT	T CTATAAACTG	TATCATTTTC TGCT	GAGGGT 1970
	GGAGTGTCC	C ATCCTTTA	A TCAAGGTGA	T TGTGATTTTG	ACTAATAAAA AAGAA	ATTTGT 2030
25						

(2) INFORMATION FOR SEQ ID NO: 49:

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 493
- 30 (B) TYPE: Nucleic acid
 - (C) STRANDEDNESS: Double
 - (D) TOPOLOGY: Linear
 - (ii) SEQUENCE KIND: cDNA to mRNA
- 35 (vi) ORIGINAL SOURCE:
 - (A) ORGANISM: Homo sapiens
 - (B) CELL KIND: Stomach cancer
 - (D) CLONE NAME: HP10424

146

	(ix) SEQUENCE CHARACTERISTICS:												
		(A)	CHARACT	ERIZATIO	N CODE:	CDS							
		(B)	EXISTEN	CE POSIT	ION: 98.	. 439							
		(C)	CHARACT	ERIZATIO	и метнор	: E							
5													
	(x	i) SEQUI	ENCE DES	CRIPTION	: SEQ ID	NO: 49	•						
	AAAGTTTC	CC AAAT	CCAGGC G	GCTAGAGG	C CCACTG	CTTC CCA	AACTACCA GCTG	AGGGGG 60					
							AC TTC TAT TT						
· 10						Met As	n Phe Tyr Le	u Leu					
						1		5					
	CTA GCG	AGC AGC	ATT CTG	TGT GCC	TTG ATT	GTC TTC	TGG AAA TAT	CGC 163					
	Leu Ala	Ser Ser	Ile Leu	Cys Ala	Leu Ile	Val Phe	Trp Lys Tyr	Arg					
		10			15	•	20						
15	CGC TTT	CAG AGA	AAC ACT	GGC GAA	ATG TCA	TCA AAT	T TCA ACT GCT	CTT 211					
	Arg Phe	Gln Arg	Asn Thr	Gly Glu	Met Ser	Ser Asr	Ser Thr Ala	Leu					
		25		30			35						
	GCA CTA	GTG AGA	CCC TCT	TCT TCT	GGG TTA	ATT AAC	AGC AAT ACA	GAC 259					
	Ala Leu	Val Arg	Pro Ser	Ser Ser	Gly Leu	Ile Asr	Ser Asn Thr	Asp					
20	40			45		50							
							TAA TAA ATT 1						
	Asn Asn	Leu Ala	Val Tyr	Asp Leu	Ser Arg	Asp Ile	e Leu Asn Asn	Phe					
	55		60			65		70					
0.5							A AAC CTC AGT						
25	Pro His	Ser Ile		Gln Lys		Leu Val	Asn Leu Ser	Met					
	0.00		75		80		85						
							A CTT AGC AAG						
	vai Giu			Glu Leu		Thr Let	Leu Ser Lys	GIÿ					
30	ምምሮ ልሮል	90		C40 000	95	400 m44	100	150					
30							AAGCGTA CAGG	450					
	Phe Arg	105	Ser Fro			Inr							
	ATGTAATG		ርፕሮርልል ል	110		TTC 4 CT	.c	402					
	oimit	O AGIG	Ologna A	OALIMAA	G ACACI	iion GT	าษ	493					
35													

- (2) INFORMATION FOR SEQ ID NO: 50:
 - (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 2044

147

	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
5		
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Epidermoid carcinoma	
	(C) CELL LINE: KB	
10	(D) CLONE NAME: HP10428	
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 288 1385	
15	(C) CHARACTERIZATION METHOD: E	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 50:	
20	AGATTCCGGC CTGGAGCTCC CAGGGCCGAG CAGACCTTGG GACCTGTGAG CGCTGCATCC	
20	AATTAACCAT GGGAAGGGTC AGCACCAGCC ACCAGCCCCT TAGGTGAGGA CTCTGCCTGG	
	GGCTCTGCTG ATGGTTCCGA ATCATGGAGC TGCAGAGAGC TCCTCCAGCC TGGAGACGTT	
	CTTGGTGAAA GCTGTGGTCT AACTCCACCG GCTCTTCCTG CACATTGTAT TCAAGAGGGG TGCCTGCCCC CGCTGACTCA GGAGCTCCGG TGCTGCAGCC GCCACGA ATG GGG AGG	
		296
25	Met Gly Arg	
	TGG GCC CTC GAT GTG GCC TTT TTG TGG AAG GCG GTG TTG ACC CTG GGG	244
	Trp Ala Leu Asp Val Ala Phe Leu Trp Lys Ala Val Leu Thr Leu Gly	344
	5 10 15	
	CTG GTG CTT CTC TAC TAC TGC TTC TCC ATC GGC ATC ACC TTC TAC AAC	392
30	Leu Val Leu Leu Tyr Tyr Cys Phe Ser Ile Gly Ile Thr Phe Tyr Asn	332
	20 25 30 35	
	AAG TGG CTG ACA AAG AGC TTC CAT TTC CCC CTC TTC ATG ACG ATG CTG	440
	Lys Trp Leu Thr Lys Ser Phe His Phe Pro Leu Phe Met Thr Met Leu	770
	40 45 50	
35	CAC CTG GCC GTG ATC TTC CTC TTC TCC GCC CTG TCC AGG GCG CTG GTT	488
	His Leu Ala Val Ile Phe Leu Phe Ser Ala Leu Ser Arg Ala Leu Val	
	55 60 65	
	CAG TGC TCC AGC CAC AGG GCC CGT GTG GTG CTG AGC TGG GCC GAC TAC	536

	Gln	Cys	Ser	Ser	His	Arg	Ala	Arg	Val	Val	Leu	Ser	Trp	Ala	Asp	Tyr	
			70					75					80				
	CTC	AGA	AGA	GTG	GCT	CCC	ACA	GCT	CTG	GCG	ACG	GCG	CTT	GAC	GTG	GGC	584
	Leu	Arg	Arg	Val	Ala	Pro	Thr	Ala	Leu	Ala	Thr	Ala	Leu	Asp	Val	Gly	
5		85					90					95					
	TTG	TCC	AAC	TGG	AGC	TTC	CTG	TAT	GTC	ACC	GTC	TCG	CTG	TAC	ACA	ATG	632
	Leu	Ser	Asn	Trp	Ser	Phe	Leu	Tyr	Val	Thr	Val	Ser	Leu	Tyr	Thr	Met	
	100					105					110	•				115	
	ACC	AAA	TCC	TCA	GCT	GTC	CTC	TTC	ATC	TTG	ATC	TTC	TCT	CTG	ATC	TTC	680
10	Thr	Lys	Ser	Ser	Ala	Val	Leu	Phe	Ile	Leu	Ile	Phe	Ser	Leu	Ile	Phe	
					120					125					130		
	AAG	CTG	GAG	GAG	CTG	CGC	GCG	GCA	CTG	GTC	CTG	GTG	GTC	CTC	CTC	ATC	728
	Lys	Leu	Glu	G1u	Leu	Arg	Ala	Ala	Leu	Val	Leu	Val	Val	Leu	Leu	Ile	
				135					140					145			
15	GCC	GGG	GGT	CTC	TTC	ATG	TTC	ACC	TAC	AAG	TCC	ACA	CAG	TTC	AAC	GTG	776
	Ala	Gly	Gly	Leu	Phe	Met	Phe	Thr	Tyr	Lys	Ser	Thr	Gln	Phe	Asn	Val	
			150					155					160				
	GAG	GGC	TTC	GCC	TTG	GTG	CTG	GGG	GCC	TCG	TTC	ATC	GGT	GGC	ATT	CGC	824
	Glu	Gly	Phe	Ala	Leu	Val	Leu	Gly	Ala	Ser	Phe	Ile	Gly	Gly	Ile	Arg	
20		165					170					175					
	TGG	ACC	CTC	ACC	CAG	ATG	CTC	CTG	CAG	AAG	GCT	GAA	CTC	GGC	CTC	CAG	872
	Trp	Thr	Leu	Thr	Gln	Met	Leu	Leu	Gln	Lys	Ala	Glu	Leu	Gly	Leu	Gln	
	180					185					190					195	
	AAT	CCC	ATC	GAC	ACC	ATG	TTC	CAC	CTG	CAG	CCA	CTC	ATG	TTC	CTG	GGG	920
25	Asn	Pro	Ile	Asp	Thr	Met	Phe	His	Leu	Gl'n	Pro	Leu	Met	Phe	Leu	Gly	
					200					205					210		
	CTC	TTC	CCT	CTC	TTT	GCT	GTA	TTT	GAA	GGT	CTC	CAT	TTG	TCC	ACA	TCT	968
	Leu	Phe	Pro	Leu	Phe	Ala	Val	Phe	Glu	Gly	Leu	His	Leu	Ser	Thr	Ser	
		•		215					220					225			
30	GAG	AAA	ATC	TTC	CGT	TTC	CAG	GAC	ACA	GGG	CTG	CTC	CTG	CGG	GTA	CTT	1016
•	Glu	Lys	Ile	Phe	Arg	Phe	Gln	Asp	Thr	Gly	Leu	Leu	Leu	Arg	Val	Leu	
			230					235					240				
	GGG	AGC	CTC	TTC	CTT	GGC	GGG	ATT	CTC	GCC	TTT	GGT	TTG	GGC	TTC	TCT	1064
	G1y	Ser	Leu	Phe	Leu	Gly	Gly	Ile	Leu	Ala	Phe	Gly	Leu	G1y	Phe	Ser	
35		245					250					255					
	GAG	TTC	CTC	CTG	GTC	TCC	AGA	ACC	TCC	AGC	CTC	ACT	CTC	TCC	ATT	GCC	1112
	Glu	Phe	Leu	Leu	Va1	Ser	Arg	Thr	Ser	Ser	Leu	Thr	Leu	Ser	Ile	Ala	
	260					265					270					275	

149

	GGC	ATT	TTT	AAG	GAA	GTC	TGC	ACT	TTG	CTG	TTG	GCA	GCT	CAT	CTG	CTG	1160
	Gly	Ile	Phe	Lys	Glu	Val	Cys	Thr	Leu	Leu	Leu	Ala	Ala	His	Leu	Leu	
					280					285					290		
	GGC	GAT	CAG	ATC	AGC	CTC	CTG	AAC	TGG	CTG	GGC	TTC	GCC	CTC	TGC	CTC	1208
5	Gly	Asp	Gln	Ile	Ser	Leu	Leu	Asn	Trp	Leu	Gly	Phe	Ala	Leu	Cys	Leu	
				295					300					305			
	TCG	GGA	ATA	TCC	CTC	CAC	GTT	GCC	CTC	AAA	GCC	CTG	CAT	TCC	AGA	GGT	1256
	Ser	Gly	Ile	Ser	Leu	His	Val	Ala	Leu	Lys	Ala	Leu	His	Ser	Arg	Gly	
			310					315					320				
10	GAT	GGT	GGC	CCC	AAG	GCC	TTG	AAG	GGG	CTG	GGC	TCC	AGC	ccc	GAC	CTG	1304
	Asp	Gly	Gly	Pro	Lys	Ala	Leu	Lys	Gly	Leu	Gly	Ser	Ser	Pro	Asp	Leu	
		325					330					335					
	GAG	CTG	CTG	CTC	CGG	AGC	AGC	CAG	CGG	GAG	GAA	GGT	GAC	AAT	GAG	GAG	1352
	Glu	Leu	Leu	Leu	Arg	Ser	Ser	Gln	Arg	Glu	Glu	Gly	Asp	Asn	Glu	Glu	
15	340					345					350					355	
	GAG	GAG	TAC	TTT	GTG	GCC	CAG	GGG	CAG	CAG	TGAG	CCAG	CCA (GGGC	AAAT		1400
	Glu	Glu	Tyr	Phe	Val	Ala	Gln	Gly	Gln	Gln							
					360					365							
	GGC'	TTAG	AAG (CAGG	CCAC'	rc c	CCAG	CCTG	C TG	CCAG	CACT	CAC	TGTG	CTC A	AAGC	CGCCAG	1460
20	GGC	TCAT	CAT (GGTA	CTG	GG A	GCTG:	rgga	G GG	GAGT	CACC	AGG	TGG T	GGG (GCCA	AGCCAG	1520
	GGA	CTCA	TGA	CTTT	rgcc	CC T	CCCT	rcag/	A GC	CTGG'	CAC	ACA	AGGG	GCG A	AGCA	CCAGGC	1580
	CAG	CCTG	GGA (CTGG	CCAG	AG C	rggg(CCCA	A GC!	rgcg(CTGG	AAT	CGCA	GCA (GGAG	AGGGGA	1640
	GTG	GGCT	GGT	TCTT	CCCA	CC A	CTTC	CCAG	CT	CTGA	CAGC	CGA	GACT	CAT S	TTCC	AAGGCA	1700
	CAG	CAGC'	TTT	CTAA	AGGG	AC TO	GAGT'	TTGG.	A CTO	GGGT'	rttg	GAC	CTCC	AGG (GGCT	GGAGCT	1760
25	TCA	TCAC	CTG	GGCA	GTGT(CT T	TTCT	CAGA	G AG	CAGG!	TTTC	TTT	ATAG'	TTT (GGAA	TAAAT	1820
	GGT	TCAC	GGT	CCAC:	rggc	CG C	CTTG!	TGTT(G CT	GGAG	ACGT	GGG	GGCA	GGG A	AGGG	GACAGT	1880
	GTG	GGCC'	TGG	CCTC	rcct'	TT C	CTTT	CCCT	G CC	TGGA(CCT	TCT	TCAA	ATG '	TCTG(GTCTTA	1940
														rcc (CCAG'	IGGGGC	2000
	CCC	ACTG	CAC	CTGC:	TGGC	AG G	AAAT	AAAT	G AA'	TGTT'	TACT	GAG'	T				2044
30																	

(2) INFORMATION FOR SEQ ID NO: 51:

35

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 1043

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

150

(vi) ORIGINAL SOURCE:

	(A) ORGANISM: Homo sapiens	
	(B) CELL KIND: Stomach cancer	
	(D) CLONE NAME: HP10429	
5		
	(ix) SEQUENCE CHARACTERISTICS:	
	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 157 837	
	(C) CHARACTERIZATION METHOD: E	
· 10		•
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 51:	
•		
	ATTAGCATAA CCCTTCCTCA GGAAGAGTGA GATTTTATAT TTGACAATA	A AGTGTTAGAC 60
	TCCATTTCTA AATACCAGAC TTCAAAAGAT AAGGTTCAAA AGTGTTATA	A GAAGATATTC 120
15	CTTTTTTTGT CCTAGAGAAC TTATTTTCCT GTGAAA ATG CCT ACC A	CA AAG AAG 174
	Met Pro Thr Th	hr Lys Lys
	1	5
	ACA TTG ATG TTC TTA TCA AGC TTT TTC ACC AGC CTT GGG TG	
	Thr Leu Met Phe Leu Ser Ser Phe Phe Thr Ser Leu Gly So	er Phe Ile
20		20
	GTA ATT TGC TCT ATT CTT GGG ACA CAA GCA TGG ATC ACC AC	
	Val Ile Cys Ser Ile Leu Gly Thr Gln Ala Trp Ile Thr Se	er Thr Ile
	25 30 35	
25	GCT GTT AGA GAC TCT GCT TCA AAT GGG AGC ATT TTC ATC AC	
25		hr Tyr Gly
	40 45 50 CTT TTT CCT CCC CAC ACT ACT CAA CAA TTC ACT CAC CAA CAA	mm ool oll occ
	CTT TTT CGT GGG GAG AGT AGT GAA GAA TTG AGT CAC GGA C	
	Leu Phe Arg Gly Glu Ser Ser Glu Glu Leu Ser His Gly Lo 55 60 65	eu Ala Glu 70
30		
	Pro Lys Lys Phe Ala Val Leu Glu Ile Leu Asn Asn So	
	75 80	85
	AAA ACT CTG CAT TCG GTG ACT ATC CTG TTC CTG GTC CTG ACT	
	Lys Thr Leu His Ser Val Thr Ile Leu Phe Leu Val Leu Se	
35		00
	ACG TCG CTG AGC TCT GGG TTT ACC TTC TAC AAC AGC A	
	Thr Ser Leu Leu Ser Ser Gly Phe Thr Phe Tyr Asn Ser I	
	105 110 115	
	- 117	

151

	CCT	TAC	CAG	ACA	TTC	CTG	GGG	CCG	ACG	GGG	GTG	TAC	ACC	TGG	AAC	GGG	558
	Pro	Tyr	Gln	Thr	Phe	Leu	Gly	Pro	Thr	Gly	Val	Tyr	Thr	Trp	Asn	Gly	
		120					125					130					
	CTC	GGT	GCA	TCC	TTC	GTT	TTT	GTG	ACC	ATG	ATA	CTG	TTT	GTG	GCG	AAC	606
5	Leu	Gly	Ala	Ser	Phe	Val	Phe	Val	Thr	Met	Ile	Leu	Phe	Val	Ala	Asn	
	135					140					145					150	
	ACG	CAG	TCC	AAC	CAA	CTC	TCC	GAA	GAG	TTG	TTC	CAA	ATG	CTT	TAC	CCG	654
	Thr	Gln	Ser	Asn	Gln	Leu	Ser	Glu	Glu	Leu	Phe	Gln	Met	Leu	Tyr	Pro	
					155					160					165		
10	GCA	ACC	ACC	AGT	AAA	GGA	ACG	ACC	CAC	AGT	TAC	GGA	TAC	TCG	TTC	TGG	702
	Ala	Thr	Thr	Ser	Lys	Gly	Thr	Thr	His	Ser	Tyr	Gly	Tyr	Ser	Phe	Trp	
				170					175					180			
	CTC	ATA	CTG	CTC	GTC	ATT	CTT	CTA	AAT	ATA	GTC	ACT	GTA	ACC	ATC	ATC	750
	Leu	Ile	Leu	Leu	Val	Ile	Leu	Leu	Asn	Ile	Val	Thr	Val	Thr	Ile	Ile	
15			185					190					195				
	ATT	TTC	TAC	CAG	AAG	GCC	AGA	TAC	CAG	CGG	AAG	CAG	GAG	CAG	AGA	AAG	798
	Ile	Phe	Tyr	G1n	Lys	Ala	Arg	Tyr	Gln	Arg	Lys	Gln	Glu	Gln	Arg	Lys	
		200					205					210					
	CCA	ATG	GAA	TAT	GCT	CCA	AGG	GAC	GGA	ATT	TTA	TTC	TGA	ATTC:	TCT :	TTCATC	850
20	Pro	Met	Glu	Tyr	Ala	Pro	Arg	Asp	Gly	Ile	Leu	Phe					
	215					220					225						
	TCA'	TTTT	GGC (GTTG	CATC	TA T	TGTA	CATC	A GC	CCTG	AGTA	GTA	ACTG	GTT A	AGCT'	TCTCTG	910
	GAC	AATT	CAG (CATG	GTAA	CG T	GACT	GTCA'	r ct	GTGA(CAGC	ATT'	TGTG'	rtt (CATG	ACACTG	970
					GCTG'	TA C	TCCT	GAAA	A TT	TTTC	CCAC	AAG	GTTG	GGG A	TAAA	GAATGG	1030
25	GAA	ATGT	CGC '	TGG													1043

(2) INFORMATION FOR SEQ ID NO: 52:

(i) SEQUENCE CHARACTERISTICS:

30 (A) LENGTH: 972

35

(B) TYPE: Nucleic acid

(C) STRANDEDNESS: Double

(D) TOPOLOGY: Linear

(ii) SEQUENCE KIND: cDNA to mRNA

(vi) ORIGINAL SOURCE:

(A) ORGANISM: Homo sapiens

(B) CELL KIND: Liver

152

(D) CLONE NAME: HP10432

5

- (A) CHARACTERIZATION CODE: CDS
- (B) EXISTENCE POSITION: 29.. 418
- (C) CHARACTERIZATION METHOD: E

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 52:

10														.=.			
10	AGAU	JAGU	sgc (GGCG	CAGU	A CC	FTGC										52
										MA /	arg (ily 8		Leu A	arg .	Arg	
	mmc.	CTC	000	CMC	CmC	O TO C	cmo	000	1	500	000	000	5	OBC	000	800	100
				CTC													100
15	Leu	10	Arg	Leu	Leu	Val	Leu 15	GIÀ	Leu	Trp	Leu		Leu	Leu	Arg	ser	
13	GTG		GGG	GAG	CAA	CCC		CCC	ACC	ccc	ccc	20	ም ረር	ccc	CCC	AGC	148
				Glu													140
	25	1114	O ₁	Olu	OIII	30	110	or,	1111	nia	35	oys	Jer	n. P	ory	40	
		TGG	AGC	GCG	GAC		GAC	AAG	TGC	ATG		TGC	GCG	TCT	TGC		196
20				Ala													
		•			45		•	•	•	50	•	•			55		
	GCG	CGA	CCG	CAC	AGC	GAC	TTC	TGC	CTG	GGC	TGC	GCT	GCA	GCA	CCT	CCT	244
	Ala	Arg	Pro	His	Ser	Asp	Phe	Cys	Leu	Gly	Cys	Ala	Ala	Ala	Pro	Pro	
				60					65					70			
25	GCC	CCC	TTC	CGG	CTG	CTT	TGG	ccc	ATC	CTT	GGG	GGC	GCT	CTG	AGC	CTG	292
	Ala	Pro	Phe	Arg	Leu	Leu	Trp	Pro	Ile	Leu	Gly	Gly	Ala	Leu	Ser	Leu	
			75					80					85				
	ACC	TTC	GTG	CTG	GGG	CTG	CTT	TCT	GGC	TTT	TTG	GTC	TGG	AGA	CGA	TGC	340
	Thr	Phe	Val	Leu	Gly	Leu	Leu	Ser	Gly	Phe	Leu	Val	Trp	Arg	Arg	Cys	
30		90					95					100					
	CGC	AGG	AGA	GAG	AAG	TTC	ACC	ACC	CCC	ATA	GAG	GAG	ACC	GGC	GGA	GAG	388
	Arg	Arg	Arg	Glu	Lys	Phe	Thr	Thr	Pro	Ile	Glu	Glu	Thr	Gly	Gly	Glu	
	105	•				110					115					120	
	GGC	TGC	CCA	GCT	GTG	GCG	CTG	ATC	CAG	TGA	CA A	TGT (GCCC	CCTG	CC A	CCGG	440
35	Gly	Cys	Pro	Ala	Val	Ala	Leu	Ile	Gln								
					125		•										
	GGC	TCGC	CCA	CTCA'	TCAT	TC A	TTCA	TCCA	T TC	TAGA	GCCA	GTC	TCTG	CCT	CCCA	GACGC	G 500
	GCG	GGAG	CCA .	AGCT(CCTC	CA A	CCAC.	AAGG	G GG	GTGG	GGGG	CGG	TGAA	TCA	CCTC	TGAGG	C 560

	CTGGGCCCAG GGTTCAGGGG AACCTTCCAA GGTGTCTGGT TGCCCTGCCT CTGGCTCCAG	620
	AACAGAAAGG GAGCCTCACG CTGGCTCACA CAAAACAGCT GACACTGACT AAGGAACTGC	680
	AGCATTTGCA CAGGGGAGGG GGGTGCCCTC CTTCCTAGAG GCCCTGGGGG CCAGGCTGAC	740
	TTGGGGGGCA GACTTGACAC TAGGCCCCAC TCACTCAGAT GTCCTGAAAT TCCACCACGG	800
5	GGGTCACCCT GGGGGGTTAG GGACCTATTT TTAACACTAG GGGGCTGGCC CACTAGGAGG	860
	GCTGGCCCTA AGATACAGAC CCCCCCAACT CCCCAAAGCG GGGAGGAGAT ATTTATTTTG	920
	GGGAGAGTTT GGAGGGGAGG GAGAATTTAT TAATAAAAGA ATCTTTAACT TT	972
10	(2) INFORMATION FOR SEQ ID NO: 53:	
	(i) SEQUENCE CHARACTERISTICS:	
	(A) LENGTH: 695	
	(B) TYPE: Nucleic acid	
	(C) STRANDEDNESS: Double	
15	(D) TOPOLOGY: Linear	
	(ii) SEQUENCE KIND: cDNA to mRNA	
	(vi) ORIGINAL SOURCE:	
	(A) ORGANISM: Homo sapiens	
20	(B) CELL KIND: Liver	
20	(C) CELL LINE:	
	(D) CLONE NAME: HP10433	
	(2, 52002 111220 11120 135	
	(ix) SEQUENCE CHARACTERISTICS:	
25	(A) CHARACTERIZATION CODE: CDS	
	(B) EXISTENCE POSITION: 73 564	
	(C) CHARACTERIZATION METHOD: E	
	·	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 53:	
30		
	AAGATTTCAG CTGCGGGACG GTCAGGGGAG ACCTCCAGGC GCAGGGAAGG ACGGCCAGGG	60
	TGACACGGAA GC ATG CGA CGG CTG CTG ATC CCT CTG GCC CTG TGG CTG GGC	111
	Met Arg Arg Leu Leu Ile Pro Leu Ala Leu Trp Leu Gly	
	1 5 10	
35	GCG GTG GGC GTC GCC GAG CTC ACG GAA GCC CAG CGC CGG GGC	159
	Ala Val Gly Val Gly Val Ala Glu Leu Thr Glu Ala Gln Arg Gly	
	15 20 25	
	CTG CAG GTG GCC CTG GAG GAA TTT CAC AAG CAC CCG CCC GTG CAG TGG	207

154

									-								
	Leu	Gln	Val	Ala	Leu	Glu	Glu	Phe	His	Lys	His	Pro	Pro	Va1	Gln	Trp	
	30					35					40					45	
	GCC	TTC	CAG	GAG	ACC	AGT	GTG	GAG	AGC	GCC	GTG	GAC	ACG	CCC	TTC	CCA	255
	Ala	Phe	Gln	Glu	Thr	Ser	Val	Glu	Ser	Ala	Val	Asp	Thr	Pro	Phe	Pro	
5					50					55					60		
	GCT	GGA	ATA	TTT	GTG	AGG	CTG	GAA	TTT	AAG	CTG	CAG	CAG	ACA	AGC	TGC	303
	Ala	Gly	Ile	Phe	Va1	Arg	Leu	Glu	Phe	Lys	Leu	Gln	Gln	Thr	Ser	Cys	
				65					70					75			
	CGG	AAG	AGG	GAC	TGG	AAG	AAA	CCC	GAG	TGC	AAA	GTC	AGG	CCC	AAT	GGG	351
10	Arg	Lys	Arg	Asp	Trp	Lys	Lys	Pro	G1u	Cys	Lys	Val	Arg	Pro	Asn	Gly	
			80					85					90				
	AGG	AAA	CGG	AAA	TGC	CTG	GCC	TGC	ATC	AAA	CTG	GGC	TCT	GAG	GAC	AAA	399
	Arg	Lys	Arg	Lys	Cys	Leu	Ala	Cys	Ile	Lys	Leu	Gly	Ser	Glu	Asp	Lys	
		95					100					105					
15	GTT	CTG	GGC	CGG	TTG	GTC	CAC	TGC	CCC	ATA	GAG	ACC	CAA	GT _. T	CTG	CGG	447
	Val	Leu	Gly	Arg	Leu	Val	His	Cys	Pro	Ile	Glu	Thr	Gln	Val	Leu	Arg	
	110					115					120					125	
	GAG	GCT	GAG	GAG	CAC	CAG	GAG	ACC	CAG	TGC	CTC	AGG	GTG	CAG	CGG	GCT	495
	Glu	Ala	Glu	Glu	His	Gln	Glu	Thr	Gln	Cys	Leu	Arg	Val	Gln	Arg	Ala	
20					130					135					140		
	GGT	GAG	GAC	CCC	CAC	AGC	TTC	TAC	TTC	CCT	GGA	CAG	TTC	GCC	TTC	TCC	543
	Gly	Glu	Asp	Pro	His	Ser	Phe	Tyr	Phe	Pro	Gly	Gln	Phe	Ala	Phe	Ser	
				145					150					155			
	AAG	GCC	CTG	CCC	CGC	AGC	TAAC	GCCA	GCA (CTGA	GCTG	CG TO	GGTG	CCTC			590
25	Lys	Ala	Leu	Pro	Arg	Ser											•
			160														
	CAG	GACC	GCT (GCCG	GTGG'	TA A	CCAG	TGGA	A GA	CCCC	AGCC	CCC	AGGG	AGA (GGAC	CCCGTI	650
	CTA	TCCC	CAG	CCAT	GATA	AT A	AAGC'	TGCT	C TC	CCAG	CTGC	CTC!	rc				695
30																	
	(2)	INF	ORMA	TION	FOR	SEQ	ID 1	NO:	54:								
		- (i) s	FOIIE	NCE	CHAR	ACTE	T C T	TCC.								

- (i) SEQUENCE CHARACTERISTICS:
 - (A) LENGTH: 1914
 - (B) TYPE: Nucleic acid
- (C) STRANDEDNESS: Double

- (D) TOPOLOGY: Linear
- (ii) SEQUENCE KIND: cDNA to mRNA

WO 98/55508

(vi) ORIGINAL SOURCE:

155

PCT/JP98/02445

				(A)	ORGA	NISM	: Ho	mo s	apie	ns							
	(B) CELL KIND: Stomach cancer																
	(D) CLONE NAME: HP10480																
5																	
	(ix) SEQUENCE CHARACTERISTICS:																
	(A) CHARACTERIZATION CODE: CDS																
	(B) EXISTENCE POSITION: 80 661 (C) CHARACTERIZATION METHOD: E																
				(C)	CHAR	ACTE	RIZA	TION	MET	HOD:	E						
10																	
	(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 54:																
ACTCTCTGCT GTCGCCCGTC CCGCGCGCTC CTCCGACCCG CTCCGCTCCG																	
																	60
	CCCC	GCGC	CG C	CCGT	CAAC											TGC	112
15								Arg	Cys			Ala	Cys	GII		g Cys	
				ama	000	1		0.004	000	400		A TO C	000	መሙር	10		160
									CTC								160
	Arg	Trp	TTE		Pro	Leu	ren	ren	Leu 20	ser	MIA	116	ALG	25	vsh	116	
20	A TP.C	ccc	CTC	15	ccc	ccc	ccc	TCC	TTG	CAG	ጥርጥ	AGC	GAC		GGC	CAG	208
20									Leu								200
	116	NIG	30		01)		01,	35	Deu	J	502	001	40		,		
	ACG	TCC		CTG	TGG	TGG	AAA		TCC	CAA	GAG	GGC	GGC	GGC	AGC	GGG	256
									Ser								
25		45			•	•	50	-				55					•
	TCC	TAC	GAG	GAG	GGC	TGT	CAG	AGC	CTC	ATG	GAG	TAC	GCG	TGG	GGT	AGA	304
	Ser	Tyr	Glu	Glu	Gly	Cys	Gln	Ser	Leu	Met	Glu	Tyr	Ala	Trp	Gly	Arg	
	60					65					70					75	
	GCA	GCG	GCT	GCC	ATG	CTC	TTC	TGT	GGC	TTC	ATC	ATC	CTG	GTG	ATC	TGT	352
30	Ala	Ala	Ala	Ala	Met	Leu	Phe	Cys	Gly	Phe	Ile	Ile	Leu	Val	Ile	Cys	
					80					85					90		
	TTC	ATC	CTC	TCC	TTC	TTC	GCC	CTC	TGT	GGA	ccc	CAG	ATG	CTT	GTC	TTC	400
	Phe	Ile	Leu	Ser	Phe	Phe	Ala	Leu	Cys	Gly	Pro	Gln	Met	Leu	Val	Phe	
				95					100					105			
35																ATC	448
	Leu	Arg	Val	Ile	Gly	Gly	Leu	Leu	Ala	Leu	Ala	Ala	Va1	Phe	Gln	Ile	
			110					115					120				
	ATC	TCC	CTG	GTA	ATT	TAC	CCC	GTG	AAG	TAC	ACC	CAG	ACC	TTC	ACC	CTT	496

	Ile Ser Leu Val Ile Tyr Pro Val Lys Tyr Thr Gln Thr Phe Thr Leu	
	125 130 135	
	CAT GCC AAC CGT GCT GTC ACT TAC ATC TAT AAC TGG GCC TAC GGC TTT	544
	His Ala Asn Arg Ala Val Thr Tyr Ile Tyr Asn Trp Ala Tyr Gly Phe	
5	140 145 150 155	
	GGG TGG GCA GCC ACG ATT ATC CTG ATC GGC TGT GCC TTC TTC TGC	592
	Gly Trp Ala Ala Thr Ile Ile Leu Ile Gly Cys Ala Phe Phe Cys	
	160 165 170	
	TGC CTC CCC AAC TAC GAA GAT GAC CTT CTG GGC AAT GCC AAG CCC AGG	640
10	Cys Leu Pro Asn Tyr Glu Asp Asp Leu Leu Gly Asn Ala Lys Pro Arg	
	175 180 185	
	TAC TTC TAC ACA TCT GCC TA ACTTGGG AATGAATGTG GGAGAAAATC GCT	690
	Tyr Phe Tyr Thr Ser Ala	
	190	
15	GCTGCTGAGA TGGACTCCAG AAGAAGAAAC TGTTTCTCCA GGCGACTTTG AACCCATTTT	750
	TTGGCAGTGT TCATATTATT AAACTAGTCA AAAATGCTAA AATAATTTGG GAGAAAATAT	810
	TTTTTAAGTA GTGTTATAGT TTCATGTTTA TCTTTTATTA TGTTTTGTGA AGTTGTGTCT	870
	TTTCACTAAT TACCTATACT ATGCCAATAT TTCCTTATAT CTATCCATAA CATTTATACT	930
	ACATTTGTAA GAGAATATGC ACGTGAAACT TAACACTTTA TAAGGTAAAA ATGAGGTTTC	990
20	CAAGATTTAA TAATCTGATC AAGTTCTTGT TATTTCCAAA TAGAATGGAC TTGGTCTGTT	1050
	AAGGGCTAAG GAGAAGAGGA AGATAAGGTT AAAAGTTGTT AATGACCAAA CATTCTAAAA	1110
	GAAATGCAAA AAAAAAGTTT ATTTTCAAGC CTTCGAACTA TTTAAGGAAA GCAAAATCAT	1170
	TTCCTAAATG CATATCATTT GTGAGAATTT CTCATTAATA TCCTGAATCA TTCATTCAG	1230
	CTAAGGCTTC ATGTTGACTC GATATGTCAT CTAGGAAAGT ACTATTTCAT GGTCCAAACC	1290
25	TGTTGCCATA GTTGGTAAGG CTTTCCTTTA AGTGTGAAAT ATTTAGATGA AATTTTCTCT	1350
	TTTAAAGTTC TTTATAGGGT TAGGGTGTGG GAAAATGCTA TATTAATAAA TCTGTAGTGT	1410
	TTTGTGTTTA TATGTTCAGA ACCAGAGTAG ACTGGATTGA AAGATGGACT GGGTCTAATT	1470
	TATCATGACT GATAGATCTG GTTAAGTTGT GTAGTAAAGC ATTAGGAGGG TCATTCTTGT	1530
	CACAAAAGTG CCACTAAAAC AGCCTCAGGA GAATAAATGA CTTGCTTTTC TAAATCTCAG	1590
30	GTTTATCTGG GCTCTATCAT ATAGACAGGC TTCTGATAGT TTGCAACTGT AAGCAGAAAC	1650
	CTACATATAG TTAAAATCCT GGTCTTTCTT GGTAAACAGA TTTTAAATGT CTGATATAAA	1710
	ACATGCCACA GGAGAATTCG GGGATTTGAG TTTCTCTGAA TAGCATATAT ATGATGCATC	1770
	GGATAGGTCA TTATGATTTT TTACCATTTC GACTTACATA ATGAAAACCA ATTCATTTTA	1830
	AATATCAGAT TATTATTTTG TAAGTTGTGG AAAAAGCTAA TTGTAGTTTT CATTATGAAG	1890
35	TTTTCCCAAT AAACCAGGTA TTCT	1014

157

CLAIMS

- A protein comprising an amino acid sequence selected from the group consisting of the amino acid sequences of SEQ
 ID NOS: 1 to 18.
 - 2. A DNA encoding the protein according to claim 1.
- 3. A cDNA comprising a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 19 to 36.
 - 4. A cDNA according to claim 3, which comprises a nucleotide sequence selected from the group consisting of the nucleotide sequences of SEQ ID NOS: 37 to 54.

15

20

5. An expression vector capable of in vitro translating the DNA according to any of claims 2 to 4 or expressing said DNA in an eukaryotic cell.

6. A transformed eukaryotic cell capable of expressing the DNA according to any of claims 2 to 4 to produce the protein according to claim 1.

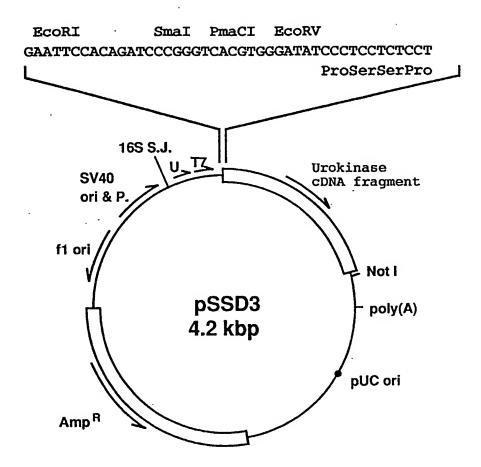
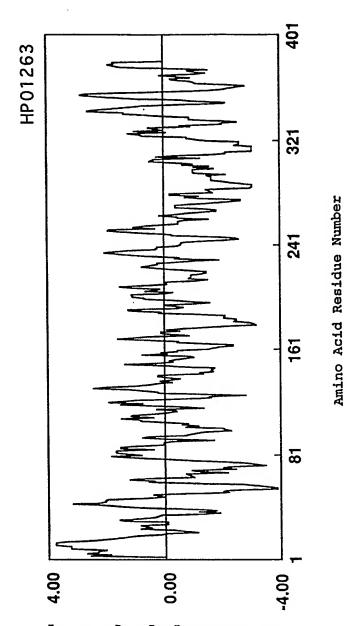


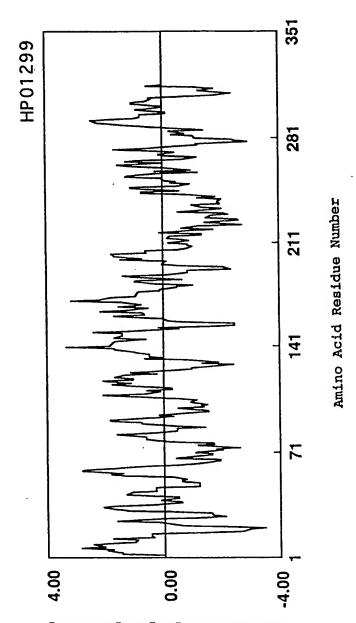
Fig.1



 ${\tt H} \lambda {\tt q} {\tt xobpopict} {\tt f} \lambda {\tt t} {\tt A} {\tt q} {\tt xobpit} {\tt fight} \lambda$

Fig.2

3/19



Ηλατοδυορίςτελ\Ηλατοδυίζετελ

Fig.3

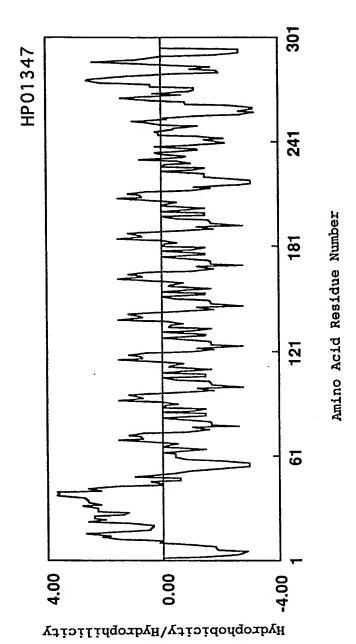


Fig.4

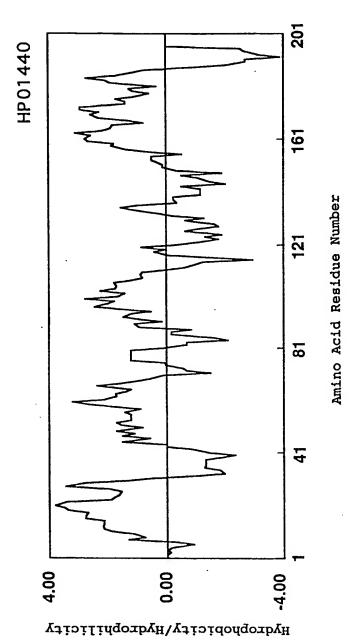


Fig.5

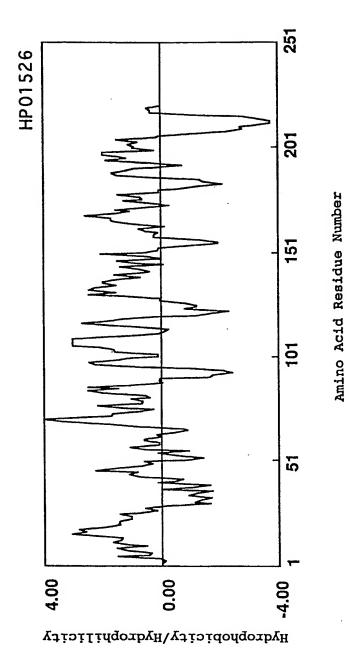


Fig.6

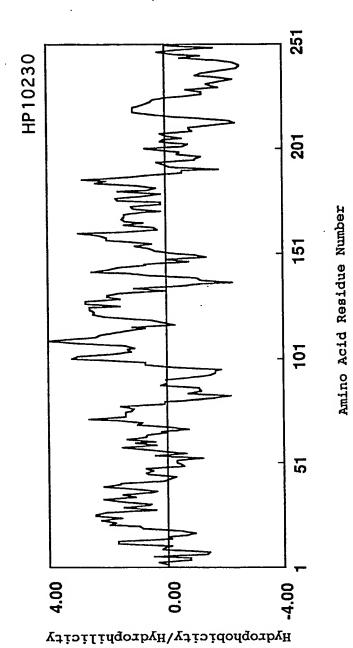


Fig.7

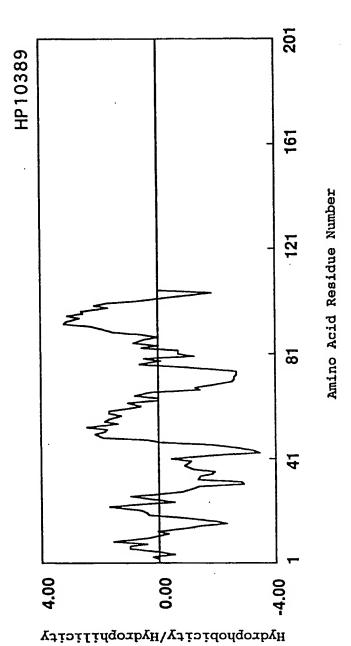


Fig.8

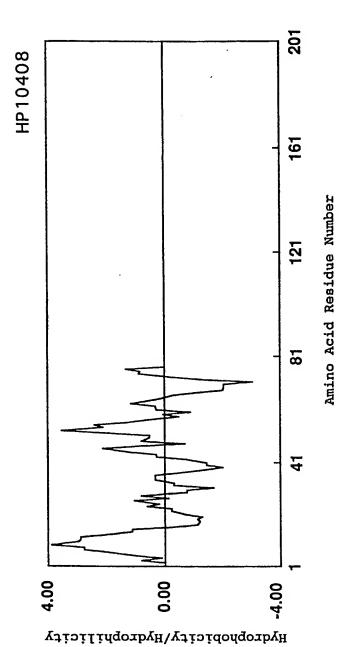


Fig.9

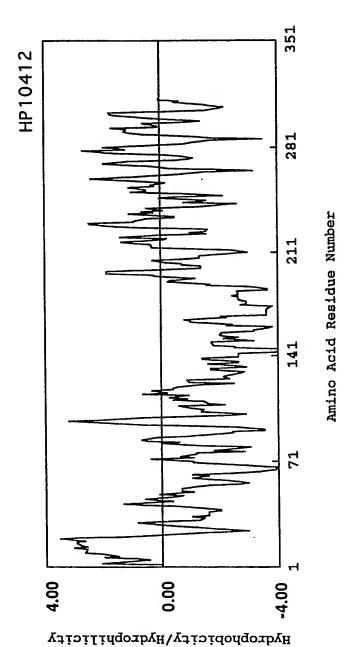


Fig.10

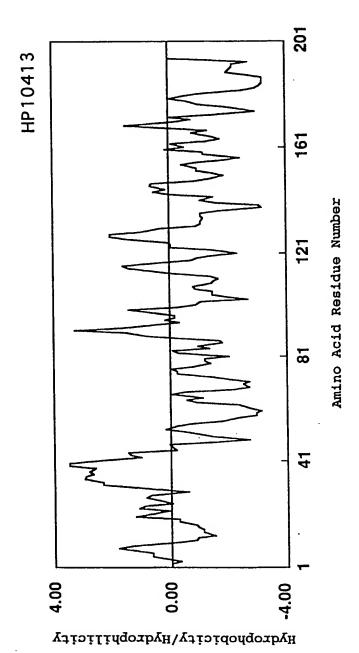


Fig.11

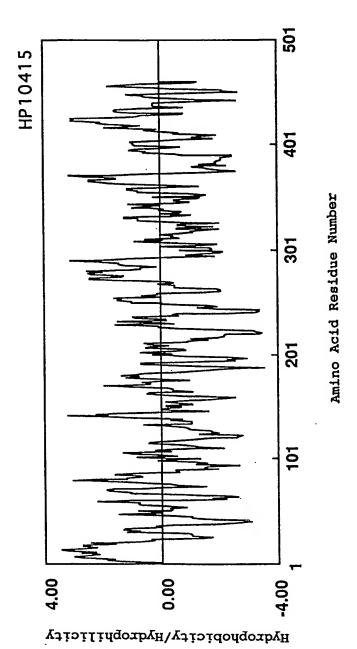


Fig.12

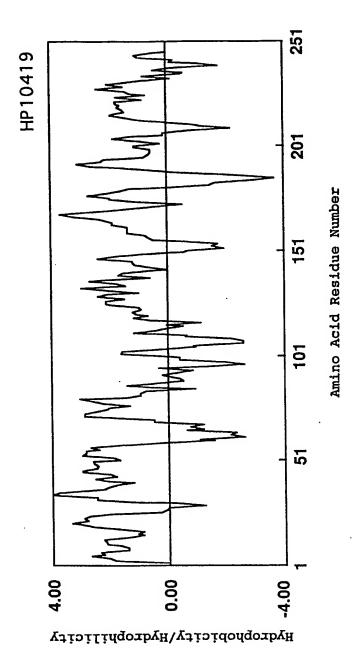


Fig.13

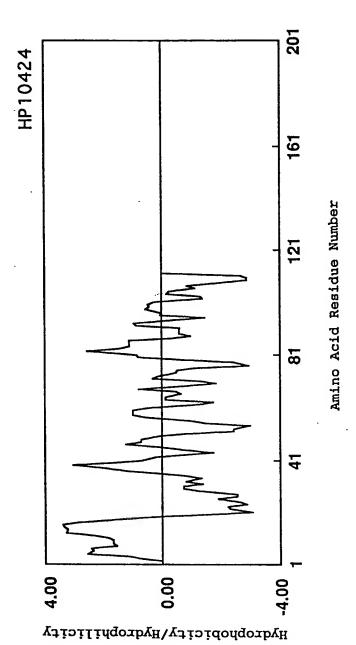


Fig.14

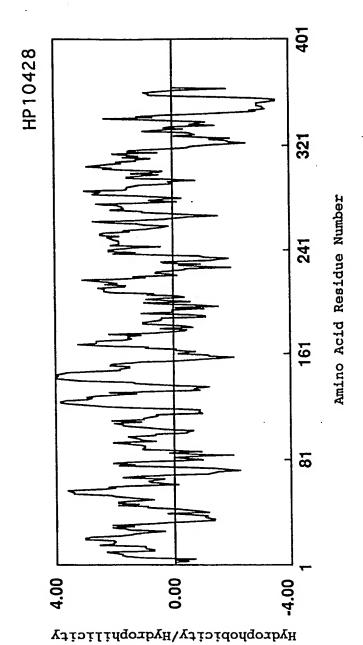


Fig.15

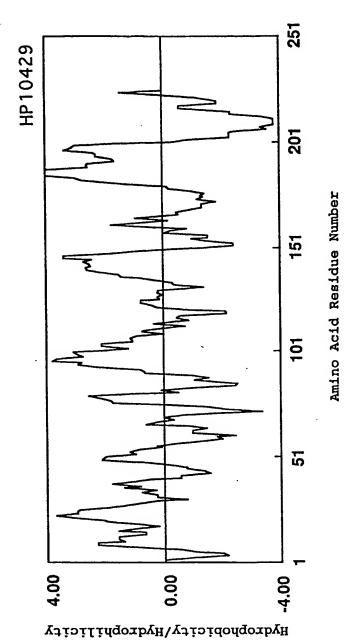


Fig.16

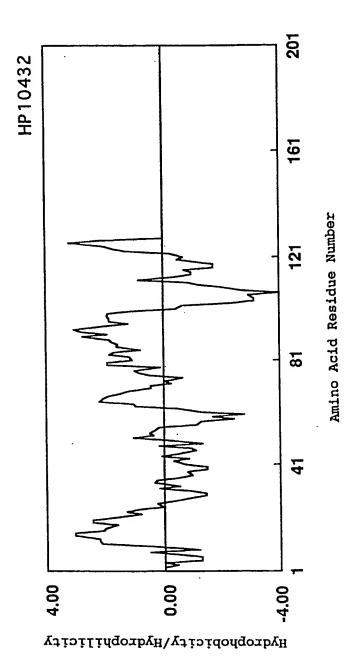


Fig.17

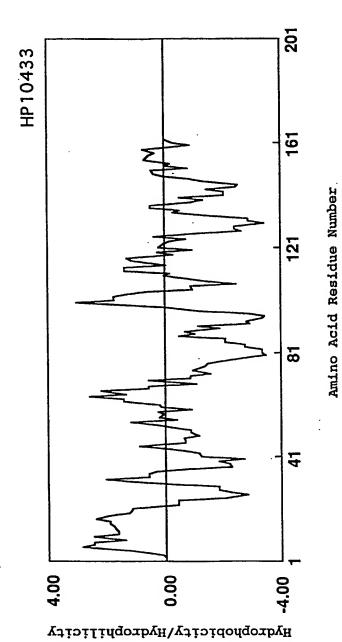


Fig.18

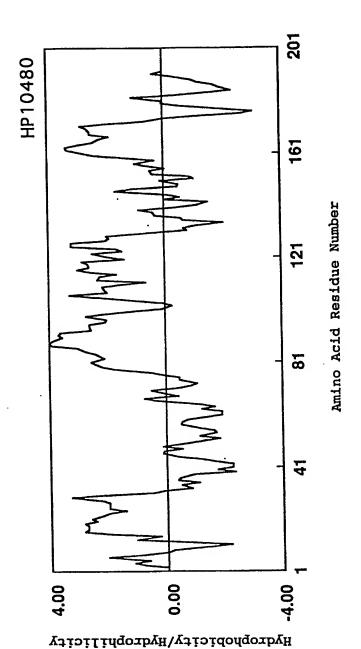


Fig.19